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Assessing the changing risk factors associated with Sudden Infant Death Syndrome.

Assessing the Changing Risk Factors Associated with Sudden Infant Death Syndrome

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Abstract

The cause of sudden infant death syndrome (SIDS) is unknown; there is no clear clinical history, no clinical signs and no definitive post-mortem findings. Until recently, SIDS was the cause of nearly half of all post-neonatal infant deaths in the UK, over 1500 deaths a year. In 1990 a strong association was found between SIDS and infants put down in the prone-sleeping position (on their front). In October 1991 the 'Back to Sleep' campaign was launched in the UK encouraging parents to lay their infants to sleep on their back. By 1994 the number of SIDS deaths dropped to 700 a year, a fall of over 50%.

However, SIDS still remains the single largest group of post-neonatal deaths. No causal mechanism has been identified to link prone position and SIDS and the effect of other factors on the decrease in incidence is unknown.

A two year case-control study, covering 12 million of the UK population, began in February 1993. A full dataset was available for 195 SIDS families and 780 matched controls. The aim of this thesis was to identify the changing epidemiological characteristics and emerging factors associated with SIDS since the dramatic fall in incidence.

The results suggest a striking reduction in the previously consistent winter peak of deaths. The previously recognised association between SIDS and socio-economic deprivation is now more marked. The adverse effects of the prone-sleeping position have been confirmed. A new finding is that side-sleeping position, previously recommended as a safer alternative, is itself associated with a possible increased risk. Exposure to tobacco smoke is a strong risk factor both during and after pregnancy and bed-sharing is a risk factor amongst mothers who smoke.

A risk-scoring system developed from this study suggests that 42% of SIDS families can be identified from 8% of the population.

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Author's Declaration

The two year case-control study described in this thesis was conducted by a large multi-disciplinary team of clinicians, scientists and researchers based in three of the old health regions: South-West, Yorkshire and Trent. The author, employed as the primary statistician, has been a main contributor to all aspects of this study. This includes helping to plan the methodology and design the questionnaire; acting as data manager for the data collection process; constructing the database; training the researchers; acting as a central resource for any problems and co-ordinating the data checking and cleaning between the three centres. The author's main responsibilities, liaising with the rest of the scientific team, have been to carry out the analysis of the results using univariable and multivariable techniques, to write up the results for reports, abstracts and peer-reviewed published papers and to present the results locally, nationally and at international conferences.

The case-control study is a collaborative effort in which the author played a central role. The research, reviews, analysis and writing up of this thesis are all the author's own work.

The views expressed in the dissertation are those of the author and not of the University of Bristol.

Peter S. Blair

Relevant Publications

Publications that have so far arisen from the work contained in this thesis :

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This thesis is dedicated to my parents, for the opportunities they were denied but managed to provide for all their children.

I keep six honest serving men,
They taught me all I knew;
Their names are what, and why, and when
And how, and where, and who.

Kipling

Contents

Page

Page

Part I

Background

Chapter 1

Introduction

Sudden infant death syndrome (SIDS), also termed "cot death" in the UK or "crib death" in the USA, is the largest single group of deaths of infants from one week to one year old in the developed world [1]. In the 1980's the postneonatal mortality rate for England & Wales was 5 infant deaths for every 1000 live births. Of those nearly half were due to SIDS. The cause of SIDS is unknown. There are characteristic post-mortem findings, but they are not diagnostic and do not yield an explanation as to why the infant died. The diagnosis is reached by exclusion, by failing to demonstrate an adequate cause of death.

The prevalence of SIDS is common to all cultures but the incidence varies. There are relatively fewer SIDS deaths in Asian and Chinese cultures but more deaths amongst indigenous cultures such as the Maoris, Aboriginal population and the Native Americans. The incidence in the UK is lower than in the white populations of New Zealand and Australia but higher than the Nordic countries. In the last 50 years many studies have been conducted to find out why these deaths occur and there is broad agreement on some of the epidemiological findings. The majority of deaths occur within the first 8 months of life, with a peak around the third and fourth month. It is more prevalent in males and the risk increases in winter months. SIDS occurs across the social strata but is more prevalent in the socio-economically deprived groups. Hospital records show that many of the SIDS infants have lower birthweight and shorter gestation. Maternal factors are important. There is a strong correlation with young maternal age and higher parity and the risk increases with multiple births. These epidemiological studies identify associations but do not identify causal sequences. Investigations into various aspects of immunology, inborn errors of metabolism and upper airways obstruction have been conducted but results have been inconclusive. In spite of much research, no one has yet been able to show exact mechanisms, although hypotheses have continued to proliferate.

Recent findings from epidemiological studies have had a dramatic effect on the incidence of SIDS. Studies in the Netherlands, New Zealand and the UK demonstrated a strong association between the prone-sleeping position (infants sleeping on their front) and the risk of SIDS. The evidence was strong enough to launch publicity campaigns in an effort to heighten public awareness of this risk. In October 1991 the "Back to Sleep" campaign was initiated in the UK. The incidence of SIDS fell dramatically from 1.7 per 1000 livebirths in 1989 to 0.7 per 1000, by 1994, a fall of 58%. Reductions of this magnitude have been found in many other countries after similar campaigns.

However, despite the dramatic fall in the number of deaths, the scale of the problem and our lack of understanding remain unchanged. SIDS now accounts for 20% rather than 50% of all postneonatal deaths, yet is still the largest single group of deaths within this age group, 3 times higher than infant mortality from congenital heart disease. The change in sleeping position is clearly a significant factor, yet there is no medical explanation as to the causal mechanism of death resulting from using the prone-sleeping position. Our current understanding and broad agreement of the epidemiological characteristics associated with SIDS families gained over the last 50 years may no longer apply to current deaths. Further studies are needed to re-assess the risk factors already established and identify any new ones that may have emerged. Given the reduction in deaths, a greater geographical area needs to be covered to maintain an adequate population base, yet the financial implications of such a welcome fall in death rate would be to reduce rather than expand resources. We therefore have a unique opportunity with this study to assess some of these changes.

In 1992 the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) was set up in the UK, funded by the Department of Health. As part of this enquiry a two year case-control study was initiated to look at Sudden Unexpected Death in Infancy (SUDI - of which SIDS deaths were the greater part), one year after the national risk-reduction campaign. It is the largest population-based SIDS study ever conducted in Europe, covering an area with approximately 12 million people, and the first to be conducted after the fall in SIDS rate.

The aim of this thesis is to assess how epidemiological characteristics and risk factors associated with SIDS have changed with the reduction in the number of deaths.

The thesis is divided into 4 parts :

- the first introductory section gives an historical perspective of the social attitudes and medical knowledge surrounding SIDS and systematically reviews the major studies conducted up to 1991 before the fall in incidence. These results are integrated using meta-analytical techniques, to quantify the main epidemiological features and yield pooled estimates for the associated risk factors. This section also introduces the CESDI SUDI study, describing the design, the possible sources of bias and the main aims of the study.
- the second section describes the analytical approach of the study, gives details of ascertainment and data quality and presents all the univariable findings of the main epidemiological features and risk factors of the primary hypotheses that have driven the study.
- the third section presents the multivariable results, using conditional logistic regression and various approaches to model design; including a two-stage empirical approach to assess all the significant univariable findings, a temporal design built to assess the variables as a sequence of events from pregnancy to death and more specific models to look at particular risks associated with the infant's environment. Two-factor analyses and stratification are also used to help interpret findings.
- finally, the fourth section summarises the shift in the epidemiology and risk factors of SIDS deaths from before the intervention campaign to what is occurring now. Preventative strategies are looked at in terms of developing both a risk score to identify future 'high risk' infants at birth and messages that can be given to both health professionals and parents.

Chapter 2

Historical perspective of SIDS

Ancient notion of overlaying

Sudden and unexpected infant deaths, unexplained by medical science, have occurred throughout history. The practice of placing infants in cots to sleep is a relatively modern phenomenon, the term 'cot death' has only recently been coined. Prior to the present century, most infants slept in bed with their parents, a practice which remains the norm in many societies today [2]. Most unexpected deaths thus occurred in bed with an adult and were attributed to overlaying of the infant by one or both parents. The earliest reference to such overlaying dates back to the First book of Kings in the Old Testament written in 500 BC

> **" and this woman's child died in the night; because she overlaid it"** [xix]

Specific advice against overlaying can be found in Roman medical text [3] instructing wet-nurses to avoid drinking or lewdness, placing the infant in the cradle along side the bed or the crib upon the bed

> **"lest unawares she roll over and cause it to be bruised or suffocated".**
>
> **Soran from Ephesos, 100 AD**

By implication, the concept of overlaying meant that the death of the infant was considered an accident and not an infanticide. The cause of death was assumed and therefore did not need to be investigated. Overlaying was not considered a secular crime but did break the fifth commandment and was therefore dealt with by the ecclesiastical courts. Several religious texts refer to this 'sin' and are primarily concerned with parental punishment.

> **"If any layman or woman overlays his or her child, [such offenders] shall do penance for an entire year on bread and water and for two years more shall abstain from wine and flesh"**
>
> **Penitential of Columban, Ireland, 600 AD** [4]

Despite the European Reformation in the 16th century, the ecclesiastical right to punish was retained in all churches. Along with penance, fines were added and the threat of partial excommunication [5]. In England it was not till the 18th century that overlaying became a concern for the secular courts. The prevention of overlaying was a matter of great concern for many scientific academies during this time. In 1732, the Royal Society in London was presented with the *arcuccio*, a cradle often used in Florence, with iron arches above the sleeping place, to prevent overlaying.

> "Every nurse in Florence is obliged to lay the child in it, under pain of excommunication"
>
> Oliver St John (FRS) [6]

By the early 19th century the medical profession recognised the causal dilemma posed by overlaying. The Births and Deaths Registration Act of 1836 required the certification of the medical cause of every death in England and Wales, yet the evidence for overlaying was mainly circumstantial [7]. Coroners such as Wakely of Middlesex, editor of the Lancet, dismissed, except very rarely, the assumption of death from overlaying and called for thorough investigation by uniform post-mortem examinations [8]. A new explanation emerged for the sudden death of an infant which was widely accepted in Europe for almost a century.

<u>The fallacy of the enlarged thymus</u>

Post-mortem examination revealed what was thought to be an enlarged thymus - a gland in the neck and upper chest, thought to compress the trachea and hinder respiration. The majority of infant post-mortems at this time were carried out on infants where death was due to malnutrition or infection, in both of whom the thymus becomes involuted and small. Thus the apparently enlarged thymus in sudden death infants was in fact the normal sized gland [9]. This was pointed out by Lee [10] as early as 1842, yet the theory proliferated in many of the medical text books as the following case of a sudden and unexpected death of an 8 month old infant, described by a practitioner in Hampstead, indicates

> "The child was always thought to be extremely healthy; it invariably however, turned on its face to sleep......The brain and all the organs were found to be healthy with the exception of the thymus gland. This occupied the entire region from the thyroid to the diaphragm..........In Osler's Medicine, under "Diseases of the Thymus Gland", it is stated that the enlargement of the gland is a recognised cause of sudden death in infants"
>
> Edward Jessop, 1905 [11]

The popular fallacy of "thymic death" continued , despite the statement of a Joint Committee of the Medical Research Council and Pathological Society of Great Britain and Ireland affording no evidence to this entity. Preventative irradiation of the thymus gland in infants was carried out in the 1930's, unwittingly causing subsequent carcinoma of the thyroid.

Accidental mechanical suffocation

Although, as a causal explanation, overlaying was no longer assumed by the beginning of this century, parents were actively encouraged to sleep their infants separately from the parental bed. In 1904, Wilcox , reviewing statistics for infant mortality, noted

> "It seems certain that amongst the poorer classes of the crowded districts of London and many of our great towns the cradle or cot for the young infant is practically unknown"
>
> Wilcox [12]

The practice of using cots was slowly adopted, yet deaths still occurred. During the 1920's there was a gradual return to the view that sudden and unexpected death in infancy was related to the sleeping environment, but this time the focus was not the parents but the sleeping attire. This shift in view to a new causal mechanism was reflected in the descriptive nomenclature of sudden unexpected deaths now described as "accidental mechanical suffocation". This was defined as simple occlusion of air passages (nose and mouth) by bedding, sleeping attire, or other mechanical means, excluding deaths from choking on solid objects or liquids. However the evidence given at inquest supporting this new definition was either circumstantial or based on external examination of the body and scene of the event. In 1926, an amendment to the Coroner's Act in England gave the coroner authority to order a post-mortem examination of sudden infant death without necessarily committing the case to an inquest if the death was thought to be from natural causes. A study by the coroner, Davison in Birmingham [13] looked at 318 infant deaths between 1938 and 1944, where accidental mechanical suffocation was suspected as a possible cause. Only 38 (12%) were confirmed after careful post-mortem examination, the remaining 280, Davison claimed, were shown to be due to natural causes, mainly bronchopneumonia sometimes associated with otitis media. Attributing such deaths to some sort of natural respiratory failure implicitly suggests the post-mortem failed to find a cause of death but at the same time exonerates the parents from any blame or having to go through the ordeal of an inquest. These findings were supported by Werne and Garrow [14], who, having investigated 167 consecutive sudden infant deaths from 1932 to 1947 in New York, failed to find one case where accidental mechanical suffocation could be the proven cause of death. In Werne and Garrow's experience, the bedclothes, often described as completely covering the face, were never close enough to prevent all access of air. Further support came from Wooley in 1945 [15], who found little evidence of suffocation at autopsy and reported the difficulty of inducing anoxemia using ordinary bedding. Wooley went on to suggest that in the light of this lack of findings

> **"To leave the family with a clear conscience is a duty secondary in importance only to saving the patient....It is therefore in keeping that we should be overly critical of a diagnosis which saddles the family with the entire blame for the death of their baby....perhaps we should be pushed so far as to admit that we are ignorant of the cause of death, thereby saving the family the stigma of having allowed their baby to smother in the bedclothes."**
>
> **Wooley, 1945**

Although no facts exist to conclusively connect the ancient notion of overlaying, the 19th century theory of an enlarged thymus or the hypothesis of accidental mechanical suffocation in the early 20th century with the syndrome we call 'cot death' today, it is highly likely that these deaths represented the same condition or conditions. Certainly some of the characteristics described by Abramson [16] of 139 infants, recorded as death due to accidental mechanical suffocation between 1939 and 1943 in New York, display a striking resemblance to the epidemiological characteristics of SIDS infants 50 years later. Three-quarters of deaths occurred between 2 and 5 months, the median age was 2 to 3 months, an excess of males, a strong winter peak, 68% slept prone and most of the families were from the lower socio-economic group. Davison also noted that quite a number of the 280 infants in Birmingham were found prone, 73% died between October and March and 74% were aged 2 to 6 months, the median age being 3 months.

SIDS - diagnosis of exclusion

In the 1950's the notion of an infant dying suddenly and unexpectedly from no known cause became accepted in the medical and scientific establishment. The term "cot death" was first coined by the pathologist Barrett in 1954.

> **"The term cot death is used here to include all cases in which an apparently healthy infant is unexpectedly found dead in its sleeping quarters, whether in a cot, pram or other kind of bed"**
>
> **Dr AM Barrett, Cambridge [17]**

His definition, however, included unexpected deaths that were later explained at post-mortem and had the added requirement that these deaths could only happen within the confines of the infants sleeping quarters. In the next decade, research into this phenomenon greatly expanded. The term "sudden death (cause unknown)" was first included as a separate category in the International Classification of Diseases (ICD 795) at the time of the eighth revision in January 1968. In Seattle, there were two international conferences, in 1963 and 1969, *looking specifically into the aetiology* (possible causes) of SIDS. The accepted nomenclature "sudden infant death syndrome" and working definition, still used today, was derived from the second of these conferences

> **"The sudden death of any *infant or young child, which is unexpected by history, and in which a* thorough post-mortem examination fails to demonstrate an adequate cause of death"**
>
> **JB Beckwith [18]**

A degree of diagnostic stability and focused research was achieved with this definition. Recognition of this syndrome changed the focus from parental blame to paths that might lead to prevention. However, in a purely scientific sense, there are problems when trying to label and define something that exists outside the periphery of current knowledge. The concept of using the compliment of what is already known may be oversimplified. No matter how comprehensive we like to think our knowledge is of any one subject, previous major discoveries suggest the essence of knowledge in both growth and direction is dynamic rather than fixed with definitive boundaries. Practical drawbacks to such a definition are two-fold. Firstly, because the diagnosis of SIDS is reached by exclusion of significant findings one is assuming the skills and knowledge of the pathologist is comprehensive and complete. The need for a precise cause of death based on imprecise medical knowledge and variation in practice may lead, in certain circumstances, to SIDS becoming a 'convenient diagnostic dustbin' [19]. Differences between countries regarding the thoroughness of post-mortem examination (in some countries the examination is not mandatory) also makes international comparison unreliable. Secondly, by using a single definition which become established over a period of time, this may lead to a reluctance in changing that definition when findings separate out different causal mechanisms. Although "syndrome" suggests a pattern of symptoms and signs, without necessarily the same cause, the temptation for the epidemiologist or medical researcher is to view SIDS as a homogeneous group [20] and analyse the data accordingly.

SIDS - the early incidence

In 1953 a steering committee was formed to investigate sudden death in infancy in the Cambridge and London areas [7], it was estimated that they would find 200 deaths per annum in England and Wales. An interim report in 1957, revealed the scale of the problem was much larger estimating 1400 deaths per year. In comparison to recent figures, there were between 1200 and 1500 deaths per year certified as being due to SIDS in England and Wales between 1980 and 1990. Given the higher number of infant births in the 1950's, the SIDS death rate at that time was around 1.6 deaths per 1000 livebirths which is comparable to rates in the 1980s ranging from 1.5 and 2.3 deaths per 1000 livebirths.

For the earlier part of this century, it is difficult to estimate the incidence of SIDS in the UK, partly because of the lack of a definition, but mainly because any statistics would be swamped numerically by the very large numbers of children dying as a result of infection and malnutrition. Some insight though can be gained from early statistics.

Wilcox [12] gives the number of infant deaths in England and Wales due to 'suffocation in bed' for the period 1889 to 1901. These were deaths of infants under 1 year old excluding those due to murder or manslaughter. The number of deaths ranged from 33 to 42 infants per million of the population during this period. To give some idea of the age distribution at this time, in 1901, 11.4% of the population were infants aged 0 to 4 years old [21]. In the 1980's, there were between 21 and 28 SIDS deaths per million, the 1981 census reports that 6.0% of the population were under 4 years old. The rates for the two periods therefore appear to be approximately the same.

A further estimate can be calculated from the 318 cases of "asphyxia", collected by Davison [13] in the 7 year period from 1938 to 1944 in Birmingham. After post-mortem examination, Davison concluded that 280 of these cases died from "natural" causes. Davison also gave the estimated population of Birmingham at that time as approximately one million people. Thus the mean number of cases in Birmingham at this time was about 40 a year, which, if projected over the population of England and Wales would give 2000 cases per annum. Using the same assumptions and calculations for the period 1918 to 1924, for which Davison also gave figures, the cases per annum for this area was twice as high. These rough approximations suggests the incidence of SIDS in the earlier part of this century in the UK was comparable if not higher than the incidence in more recent times.

SIDS - the fall in incidence

Research into SIDS vastly expanded after the 1960's and the next chapter will deal with the major findings from many of these studies. One finding, however, has to be put into historical context because of its contribution to the dramatic fall in SIDS rates world-wide. Although the association between prone-sleeping and SIDS had been noted in earlier American studies, Susan Beal of Australia was the first person to consistently investigate sleeping position in relation to cot death. After 4 years of home visits (mostly on the day of death) Beal reported in 1978 [22], that of the 126 infants she investigated, 71 (56%) were found lying face down on the mattress or pillow, of whom 14 were found prone for the first time. For the next ten years she became a main proponent of the possible risk of prone-sleeping associated with SIDS. In 1984, Saturnus published a study in Germany which supported Beal's suggestion, but this paper received very little attention [23]. A year later, Davies, in Hong Kong [24], noted that SIDS was an extreme rarity amongst the Chinese population, who routinely placed their babies supine to sleep, whilst amongst the European population the incidence was higher. A two year study carried out in the Netherlands [25] was followed in October 1987 by a major publicity campaign advising parents to lay their infant in the supine or side-sleeping position. Between 1987 and 1988, prone-sleeping halved and the SIDS rate in the Netherlands correspondingly dropped by 40%. At the same time, in November 1987, a major study began in New Zealand [26], which showed that infants had a significantly increased risk of dying if they were put to sleep on their front (73% SIDS vs 43% control infants), whilst earlier the same year a major case-control study looking at the interaction between bedding and sleeping position began in Bristol, England. The Avon Infant Mortality Study, instigated by Fleming [27], analysed the histories of 67 SIDS infants compared with 144 matched controls. They found that infants who died of SIDS were 8.8 times more likely to have slept prone and to be more heavily wrapped. These findings were independent associations. In 1989, parents in Avon were advised to change their practice accordingly which led to a fall in incidence from 3.2 per 1000 livebirths to 1.8 in 1989 and 1.2 by 1991. On the evidence of this data and similar unpublished data in New Zealand, a national campaign entitled "Back to Sleep" was launched in the UK in October 1991. The incidence of SIDS in England and Wales was 1.7 per 1000 livebirths in 1979, rose to a peak of 2.3 in 1988 and fell back to 1.7 by 1990. After the "Back to Sleep" campaign the rate dramatically fell until 1994 and remained constant at 0.7 deaths per 1000 livebirths in 1995, a drop of nearly 58%. Similar levels are now reported in both Scotland and Ireland and reductions of the same magnitude have been reported world-wide [28]. The SIDS incidence in some Nordic countries (Norway and Finland 0.6 deaths per 1000 livebirths, Sweden 0.5 and Denmark 0.3) have fallen to levels similar to countries such as Japan, China and India where the SIDS incidence has traditionally been low. In other parts of Europe the levels are more difficult to assess, partly because an intervention campaign has taken longer to organise and partly because of the lack of comparable statistics and mandatory post-mortem findings. In both Australia (1.0 deaths per 1000 livebirths) and New Zealand (1.4 deaths per 1000 livebirths) the levels used to be much higher although they still remain high amongst Maori and Aboriginal populations. A recent campaign in the United States has seen a 30% reduction to 1.1 deaths per 1000 livebirths, although again the rates remain high amongst the Native Americans. Unfortunately recent reports also state, as in the UK, that the incidence has not continued to fall but has remained at the same reduced level. Nevertheless, this fall in SIDS rate is one of the greatest achievements of medical science this century. What is surprising is the length of time it took to discover the association.

SIDS - the association with prone sleeping

Prone-sleeping is an aberration of the twentieth century. In images of art and earlier baby manuals, the sleeping infant is always shown supine or in the side position [29]. In

Soran's Roman medical text nearly 2000 years ago, advice is given to place the head of the infant in a raised position. The implication of this being that the baby is placed in a supine position, advice which is colourfully described much later in *The Nurses Guide* [30] published in London in 1729

> **"So long as a Child takes no other nourishment but milk, 'tis better he should be laid to sleep on his back, than on either of his sides. For the back is like the keel of a ship, the basis and foundation of the whole body, upon which the child may rest with safety and ease. But if he be laid on either of his sides, there is a danger that his rib-bones, which are as yet soft and tender and which are fastened by very slight ligaments, may give way and bend inward, under the weight of the whole body. But as soon as he has teeth, and begins to live on a more substantial diet, and that his bones and their ligaments are become stronger, he may then be laid to sleep sometimes on one side, and sometimes on the other, that so both of them may grow alike, and become equally strong."**

Prone-sleeping became popular in the USA in the 1920's, and in the UK in the 1960's. The reasons for adopting prone-sleeping position were diverse. Abramson in 1944 [16] states that it was common nursing practice to place the infant in the face-down position, firstly because it was believed the baby was more comfortable and fell asleep more easily, and secondly it prevented the flattening deformity of the skull. The latter assumption was based on work carried out in New York by Greene in 1930 [31]. Yet findings from Abramson's own study, published by the New York State Department of Health a year later [32], reported explicitly that the posture most frequently noted of all infants found dead due to accidental mechanical suffocation, was in the face-down position (68%). Around the same time, Werne and Garrow [14] postulated that by placing the infant in the prone position, postural drainage of infected secretions from the tracheobronchial tree may lessen the likelihood of pneumonia. In 1961, an editorial in the British Medical Journal suggested that sleeping supine led to a faulty alignment of the feet [33]. In 1973, a diagram listing the disadvantages of the supine position and advantages of prone can be found in the *Acta Paediatrica Scandinavia Journal* [34] based on work by Reisetbauer and Gleiss. According to the authors, the supine position decreased the opportunity for perception and experience of the infant, with a danger of aspiration. During this period, special care neonatal units were quickly expanding and a number of publications appeared showing the apparent benefits for pre-term infants in sleeping prone [35], benefits that included better gastric emptying [36], better oxygenation [37, 38] and more effective ribcage and abdominal coupling, with a decreased work of breathing [39]. However, these publications, which seemed to influence healthcare professionals in the UK, led to the incorrect assumption that what was best for the pre-term infant would therefore be best for the normal, full-term infant. According to Beal [40] the practice of prone-sleeping (or to be more precise, periods of lying unobserved in the prone position) was actively encouraged in most countries in the 1960's and 1970's, and rose dramatically: 40 % in Australia, 57% in Avon, UK, 62% in the Netherlands and 65% in Norway. She argues that countless SIDS deaths had to occur for us to find out that prone sleeping was a problem. The earliest published European studies had too few prone infants to notice the importance of the position; the earliest American studies had too many.

Chapter 3

Integrating study results

The traditional narrative research review

Seldom would results from one definitive study, no matter how large or well-conducted, be enough to prove or disprove a set of null hypotheses. With epidemiological studies in particular, where complex factors need to be measured outside laboratory conditions, confirmation of findings is needed from several further studies. Replication of experimental results has long been a central feature of scientific inquiry but this raises questions of how to combine the results obtained. The number of SIDS studies has grown exponentially since the 1960's and meticulous attention has been paid to the scientific methodology and interpretation of results. However, the same approach has not been taken with the integration of these results, the portrayal of the accumulated knowledge largely being described with narrative research reviews. These traditional reviews are prone to subjective interpretation, crude classifications, and the use of what Light and Smith [41] refer to as the 'voting method' which is inherently flawed. The 'voting method' involves classifying a particular finding in each study as significantly positive, significantly negative or of no significant relationship, consistency being achieved if the finding from each of the studies falls mainly into one of these three classifications. This method measures the direction of the finding but takes no account of its strength, and in spite of its intuitive appeal, the bias in this method does not reduce as the number of studies increases and may ultimately lead to the wrong conclusions [42]. A study conducted by Jackson [43] on the practices and methods of research reviewers, sampling at random 36 reviews from leading journals, concluded that reviewers frequently eliminate studies from consideration because of *a priori* judgements, often focus their discussion disproportionately, fail to examine previous reviews on similar or the same topics, fail to recognise sampling error placing further significance on chance findings and usually report so little about their methods of reviewing that the reader cannot judge the validity of their conclusions. Clearly there is a need for a more scientific approach to integrating the results from multiple studies. The name, given by Glass [44], to this needed systematic review is *meta-analysis*.

Meta-analysis

Meta comes from the Greek word meaning after or beyond, chosen to distinguish the integration of results from the *primary* or *secondary* analyses conducted on individual studies. *Meta-analysis* is the statistical analysis of the findings of many individual analyses or the analysis of analyses. In essence, it involves a structured search for the necessary studies and a standardised measure that reflects both the strength and direction of particular findings. An informative and straightforward measure proposed by Glass [45] in 1976 was to take the mean difference between experimental and control groups divided by the within-group standard deviation, termed the *effect size*. For epidemiological case-control and cohort studies, graphical displays of the odds ratios or relative risks are often used, marked by a circle or tick and 95% or 99% confidence limits about the estimate are displayed as straight lines extending to the left and right of the point estimate. The lines for each study appear one above the other, and the last line indicates the value of the summary estimate pooled across all individual studies along with its confidence interval. Several alternative methods can be used [46]. For this analysis, results from both case-control and cohort studies were utilised. The effect of combining results from both types of study can yield an erroneous summary estimate, weighted towards the prevalence of risk factors amongst extremely large control populations, often used in cohort studies and sometimes used in case-control studies. Two alternative summary measures will therefore be used; a summary estimate pooled across all case-control studies, where the controls are not part of a large cohort, and a summary estimate from all studies weighted by the number of cases in the case-control or cohort study (the individual study estimates being converted from the log scale before the weights are calculated). The initial pooled estimate will have tighter confidence intervals but will be more sensitive to the prevalence of risk factors in each population, whilst the weighted estimates are not influenced by the prevalence but will have wider confidence intervals and be more sensitive to the number of cases evaluated in each study.

There are, however, substantive issues in using *meta-analysis* that need to be addressed. Firstly, there is the problem of publication bias or the *file-drawer phenomenon* [47] ie there is a tendency on an author's part not to submit for publication a finding, or may be a whole article, that fails to show an effect. This is difficult to overcome although the bias may be reduced if time is spent trying to recover findings from unpublished data. Secondly there is the problem of integrating studies of varying quality. The psychologist and philosopher HJ Eysenck [48] describes the practice of including methodologically inadequate research as "mega-silliness". It is intrinsic however, to this method of integration that the influence of study quality has been regarded as an empirical *a posteriori* question, not an *a priori* matter of opinion or judgement used to exclude large numbers of studies from consideration. Finally, as this integration is based on summary statistics from published papers, rather than raw data, the analysis will be limited by the consistency of analytical technique used in the primary analysis and the statistics that are reported. Many epidemiological studies quite rightly adjust significant findings for other confounding factors, but rarely will the same confounding factors be used in each different study. Attempts have been made to produce guidelines to standardise methods of technique and reporting [49-51] which may reduce the problem in the future. Current attempts at meta-analysis can only report the unavailability or lack of consistency as missing values. The problems discussed here are not unique to meta-analysis but to all integrating methods. Perhaps as we strive for statistical rigour, present meta-analyses serves as a *glasnost*, opening up the review procedure to overcome problems that have long been hidden.

Types of study design

Several epidemiological study designs are used in medical research. In this particular field five designs have been utilised. Some studies may not fit exactly in to a particular design described, these categories are not strict definitions but give some idea of the methods used for data collection :

(i) Case-control design with future incidence identification

The data is collected retrospectively (and therefore would be described as a 'retrospectively' designed study) but the cases and controls are identified prospectively. A population area is chosen and information collected as the SIDS cases are identified over a specified time period. A notification network is required, which can be expensive and time-consuming to set up, but an efficient network can maximise case ascertainment and potentially reduce recall bias if the families are contacted soon after the event.

Control infants are chosen, sometimes matched by certain criteria, but intrinsically utilising a randomised selection procedure. Preferably the controls are normal healthy infants chosen from the community, although hospitalised infants are sometimes used to decrease cost and maximise the response rate. Families can be interviewed or contacted by post. The latter method is cheaper but suffers from poor response rates in terms of the number of questionnaires returned and the number of questions answered correctly. Information from medical records is also usually collected.

(ii) Case-control design with retrospective identification

Similar to the design above but with the cases being identified retrospectively. Using hospital records or some sort of register, SIDS families are contacted after the event. A notification network is not required, reducing cost, but potentially could suffer from recall bias if the time from death to contact is quite long. Control families can be chosen in the same way, but more usually contemporary control families are chosen as the study is being carried out. This can obviously lead to problems given the changing parental practices regarding the infant, illnesses in the community and shifts in demography. Sometimes, especially in large countries such as the United States, the interviews are conducted by telephone, which has implications in terms of sample bias.

(iii) Nested case-control design

In this design the cases and controls are chosen from a cohort of the population from which data has already been collected. This design is limited in that comparisons can only be made with the specific information collected earlier from the cohort population.

(iv) Prospective cohort design

Populations are studied for a specified length of time, usually for a number of years, and information is gathered at specified time intervals. In this design, both data gathering and case identification are carried out prospectively. The type of information collected will evolve depending on the families' circumstances. Control infants are taken from a subset or sometimes the whole cohort excluding the SIDS cases. This is an expensive design but eliminates many of the biases inherent in other designs. To effectively gather information on SIDS families, the population covered has to be extremely large.

(v) Historical cohort design

In SIDS research this design is mainly used as a data collection exercise from medical records. It is, in some sense, the most flawed design. Not only is one limited by the type of information collected, but one has no control over **how** that data was collected. These studies, using large cohorts, generate risk estimates with impressively narrow confidence intervals but are much more difficult to interpret.

Previous SIDS studies

Before embarking on time-consuming and costly studies in any medical field, it is important to assess previous evidence from earlier studies as this will both avoid looking at factors already established and provide leads as to where the research should be going. Not only is this a relatively quick and cheap exercise, it would be unethical not to do so. In the field of SIDS research there have been several reviews but no systematic attempt to compile a definitive list of previous studies. To this end a fairly comprehensive search for SIDS epidemiology studies was undertaken.

The search was for all epidemiological SIDS studies from 1950. The inclusion criteria were set to a minimum in that any epidemiological survey was included that compared at least two groups, one of which could broadly be defined as SIDS infants. The only exclusion criteria for this thesis were non-English written papers because of the constraints on time and resources. The search strategy along with references to the excluded papers are outlined in Appendix I.

From 1950 until the beginning of the CESDI SUDI study in 1993 a total of 74 studies were found, twice the number listed in any previous review. Table 1.1 lists 51 case-control studies, Table 1.2 a further 23 case-series and cohort studies.

These investigations were conducted in 17 countries: 20 from the United States, 19 from Australasia and 15 from the United Kingdom alone. Amongst these studies medical records from over 28,000 SIDS infants have been analysed and further information collected from over 4000 of the SIDS families. Some of the studies concentrated on broader epidemiological aspects, others looked in more detail at one particular factor. There were 38 studies where information was collected directly from the SIDS and control families of which 31 were by interview with the families, 6 were by postal questionnaire (*9, 10, 45, 47, 51 61*) and one by telephone interview (*49*).

Table 1.1 - SIDS case-control studies from 1950 to 1993					
St No	*First author* [Reference]	Place of Study	Study Period	SIDS	Controls
1	*Bierling-Sorensen F* [52]	Copenhagen,Denmark	1956-71	139	524
2	*Krauss JF* [53]	US (multi-centre)	1959-66	193	1930
3	*Naeye RL* [54]	US (multi-centre)	1959-66	125	375
4	*Steele R* [55]	Canada	1960-61	80	157
5	*Protestos CD* [56,57]	Sheffield, UK	1960-72	94	94
6	*Froggatt P* [58,59]	Northern Ireland	1965-67	162	162
7	*Fedrick J* [60-63]	Oxford, UK	1966-70	170	510
8	*Rintahuka PJ* [64]	Finland	1969-80	311	297
9	*Schrauzer GN* [65]	San Diego, US	1970-72	108	137
10	*Bergman AB* [66]	Washington State, US	1970-74	56	86
11	*Tonkin SL* [67]	Auckland, NZ	1970-82	91	1882
12	*Golding J* [68,63]	Oxford, UK	1971-75	167	501
13	*Carpenter R* [69,70]	Sheffield, UK	1972-76	195	250
14	*Luke JL* [71]	Columbia District, US	1973-76	92	100
15	*Getts AG* [72]	Nebraska, US	1973-78	176	43
16	*Buck GM* [73-75]	New York, US	1974	151	355
17	*Williams AL* [76]	Australia	1974-82	763	1341
18	*Knoweldon J* [77-80]	UK (multi-centre)	1976-79	303	277
19	*Kahn A - 1* [81]	Belgium & France	1977-82	95	65
20	*Kahn A - 2* [82]	Belgium & France	1977-84	45	84
21	*Hoffman HJ* [83-85]	US (multi-centre)	1978-79	757	1514
22	*Wagner M* [86]	France	1978-81	207	136
23	*Matthews TG* [87]	Dublin, Ireland	1979-80	34	34
24	*Stebbens VA* [88]	UK (multi-centre)	1979-81	13	478
25	*Taylor EM* [89,90]	Sheffield, UK	1979-82	26	52
26	*Nelson EAS - 1* [91,92]	New Zealand	1979-84	377	936
27	*Cameron MH* [93]	Melbourne, Australia	1980-82	225	411
28	*de Jonge GA* [25]	Netherlands	1980-86	106	567
29	*McGlashan ND* [94]	Tasmania, Australia	1980-86	167	501
30	*Alessandri LM* [95, 96]	Western Australia	1980-88	66	337
31	*Einspieler C* [97]	Styria, Austria	1982-86	120	80
32	*McLoughlin A* [98]	Tameside, UK	1982-86	50	100
33	*Wierenga H* [99]	Netherlands	1983	15	30
34	*Karagas MR* [100]	Washington State, US	1984-88	728	3021
35	*Li D-K* [101]	Washington State, US	1984-89	855	3464
36	Beal SM [102]	South Australia	1985-89	100	220
37	Buve A [103]	England & Wales	1986	1100	5869
38	*Flahault A* [104]	France	1986	228	405
39	*Lee N* [105]	Hong Kong	1986-87	16	32
40	*Nelson EAS - 2* [106-108]	Dunedin, NZ	1986-87	135	4041
41	*Kelmanson IA* [109]	St Petersburg, Russia	1986-91	30	42
42	*Bartholomew A* [110]	Scotland	1987	79	79
43	*Fleming PJ* [27,111-113]	Avon & Somerset,UK	1987-89	72	144
44	*Mitchell EA - 1* [114-129]	New Zealand	1987-90	440	1652
45	*Gormally S* [130]	Ireland	1987-91	97	98
46	*Schoendorf KC - 1* [131]	US (multi-centre)	1988	201	3575
47	*Schoendorf KC - 2* [131]	US (multi-centre)	1988	234	2844
48	*Ponsonby A-L* [132-134]	Tasmania, Australia	1988-90	43	86
49	*Klonoff-Cohen H* [135-137]	California, US	1989-92	200	200
50	*Wigfield R* [138, 139]	Avon & Somerset, UK	1990-91	32	216
51	*Mitchell EA-2* [140-143]	New Zealand	1993	174	1077
Shaded studies represent those where information was only gathered from medical records					

Table 1.2 - SIDS cohort & case-series studies from 1950 to 1993

St No	*First author* [Reference]	Place of Study	Study Period	SIDS	Controls
52	*Lewak N* [144]	Oakland, US	1960-67	34	14823
53	*Bergman AB* [145]	Washington State, US	1965-67	120	57937
54	*Murphy J* [146]	United Kingdom	1965-77	96	46412
55	*Irgens LM* [147]	Norway	1967-80	1062	2520
56	*Øyen N* [148]	Norway	1967-88	1984	1235789
57	*Kraus JF* [149]	California, US	1968	573	1138
58	*Newman MN* [150]	Tasmania, Australia	1975-81	213	48240
59	*Ponsonby A-L* [151]	Tasmania, Australia	1975-87	348	55944
60	*Bartholomew S* [152]	Scotland	1977-85	279	79
61	*VandenBerg M* [153]	New Zealand	1978-79	151	51602
62	*Adams MM* [154]	United States	1979-81	2100	1486051
63	*Malloy MH* [155]	Missouri, US	1979-83	372	305370
64	*Bouvier-Colle MH* [156]	France	1979-85	8432	21866
65	*Borman B* [157]	New Zealand	1981-83	630	151474
66	*Tonkin SL* [158]	New Zealand	1981-85	192	4041
67	*Haglund B* [159]	Sweden	1983-85	179	260908
68	*Bauchner H* [160]	Boston, US	1984-86	5	991
69	*Irwin KL* [161]	Washington State, US	1984-88	284	114250
70	*Kilkenny M* [162]	Victoria, Australia	1985-89	601	307451
71	*Durand DJ* [163]	California, US	1987-89	18	7075
72	*Dwyer T - 1* [164]	Tasmania, Australia	1988-90	15	116
73	*Dwyer T - 2* [165]	Tasmania, Australia	1988-92	39	6233
74	*Fujita T* [166]	Japan	1989	88	409591

Shaded studies represent those where information was only gathered from medical records

NB Because the results of some studies are reported in several papers, future reference to the 74 studies in this section will be made by the italicised study number in the left-hand column of the above tables, with round brackets to distinguish from the square bracketed non-italicised usual references.

One of the earlier studies (*4*) included deaths due to respiratory infection in the SIDS group and another (*57*) included all sudden unexplained deaths.

Most of the studies used live control infants matched on certain factors, 5 studies (*15, 30, 42, 55, 57*) used other infant deaths as the control group while 3 studies (*16, 17, 24*) used both live and dead control groups. One study (*19*) used near-miss SIDS cases for controls, another (*20*) used the surviving twin of the SIDS infant.

Several of the investigations were conducted with a very small number of SIDS infants, some had obvious methodological flaws such as very low response rates (*9, 10, 45*), or used different interview techniques for the cases and controls (*8, 11, 36*). In less than half of these studies was information gathered directly from the families. Some of the studies present only univariable statistics whilst others only present multivariable statistics (controlling the factor being measured for other risk factors). Different significance tests were used and different cut-off points were used for categorical data. However, results from all of the studies will be integrated, and interpretation of the results, including any methodological differences, will be looked at in terms of specific factors measured.

The following two chapters will look at some of the common epidemiological characteristics and risk factors associated with SIDS infants. Given the number of studies, the number of factors and the complexity of each analysis, the following description will serve as a brief outline to the wealth of detail presented in each paper.

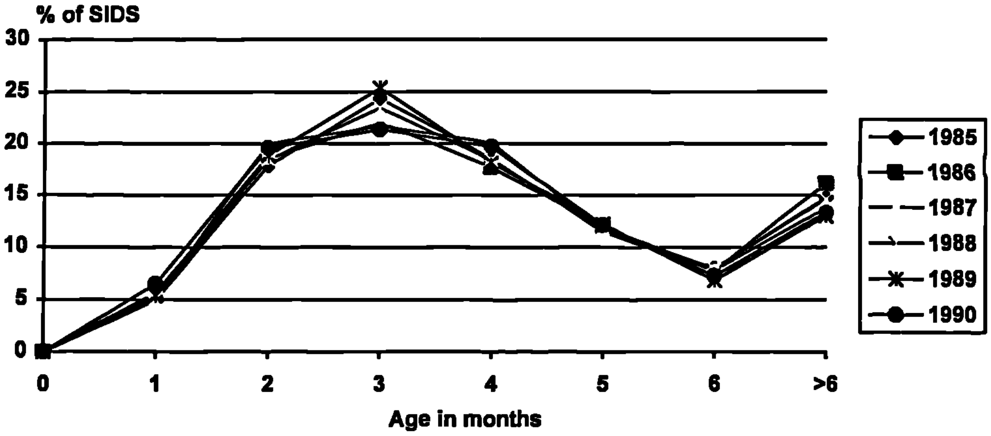
Chapter 4

Epidemiological features before the fall in incidence

Age distribution

The age distribution in Figure 1.1 (supplied by the Office of Population and Census & Surveys (OPCS) now known as the Office for National Statistics (ONS)) shows the distribution for all sudden infant deaths in England and Wales in the 6 year period before the intervention campaign.

Figure 1.1 Age distribution of sudden infant deaths in England & Wales 1985-90



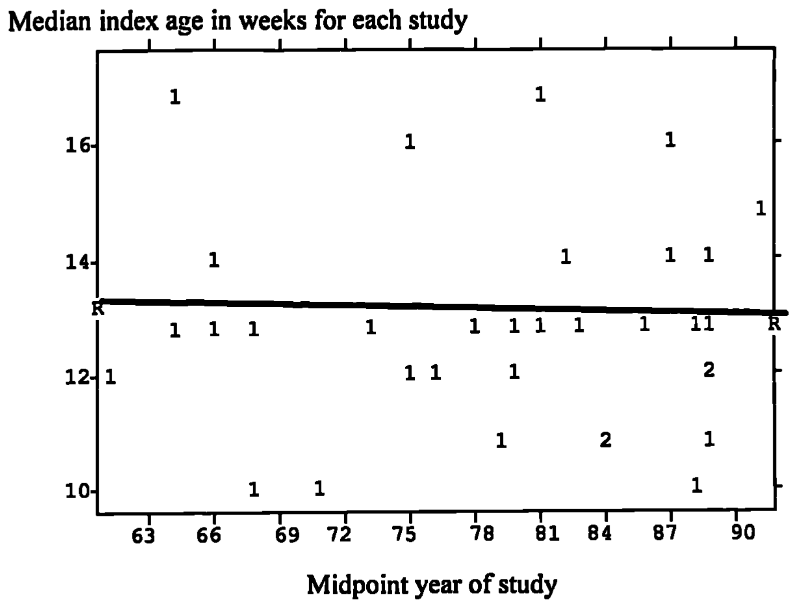
Source : OPCS health & population monitor [167, 168]

This distribution is characteristic of SIDS during this period: a relative immunity in the first 3 weeks of life, a large peak between 2 and 4 months and very few deaths after 6 months (unfortunately the data was not broken down after the first 6 months). National statistics from many other countries show a similar characteristic age pattern. This is markedly different from the age distribution of all infant deaths where both Kraus and Wagner (*2 & 22*) show in their studies that most deaths occur within 28 days and a greater number after 6 months, even if we take into account the marked differences in the first few weeks the difference between the distribution remains significant. This is further demonstrated by Bouvier-Colle (*64*) showing that deaths from congenital malformations decrease steadily from early age , whilst deaths from respiratory or infectious diseases remain relatively constant over the first year of life.

National statistics are difficult to obtain before 1980 because of the recent addition of SIDS as a separate cause of death to the International Classification of Diseases *in 1979.* They are also solely reliant on post-mortem classification, which is not always accurate. The individual studies however, stretch back much further and greater attention is often paid to the classification of death. These studies can be used to approximate whether the age distribution has significantly changed over the last 30 years.

The average age of SIDS infants was given or could be calculated from 33 studies (many of the studies had matched for age and therefore did not present a quantifiable statistic for this factor). Most reporters quoted the median age although 7 incorrectly reported the mean which gives a slight over-estimate because of the skewness of the age distribution, 3 studies only included deaths over 28 days of age which again will give a slight over-estimate. Despite these discrepancies, the median age given in each study narrowly spanned 10 weeks to 17 weeks, the most common being 13 weeks, none of the studies suggesting a departure from the distribution shown in Figure 1.1. Plotting the median age from each study against the mid-point year of each study period we can see if there has been a change in peak incidence between 1961 and 1991.

Figure 1.2 - Median age of SIDS plotted against year of study



N=33 studies

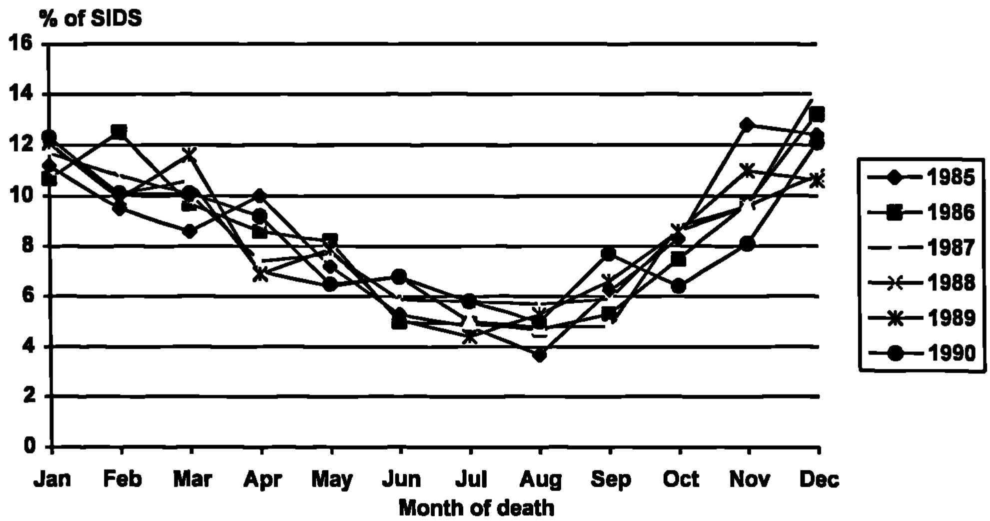
Figure 1.2 shows an almost horizontal regression line (Pearson's correlation coefficient =

-0.03, p=0.89), suggesting the peak incidence has remained constant over this time period. Within specific subgroups there was some variation. Hoffman (*21*) showed that black infants were significantly younger than white infants which was also demonstrated in the Aboriginal population by Alessandri (*30*). Both Ponsonby (*59*) and Adams (*62*) found that pre-term infants (< 36 weeks) and those with low birthweight, (< 2500g) died at an older median age. Malloy (*63*) also found that infants exposed to tobacco smoke also died at an older age.

Seasonal occurrence

Figure 1.3 shows the percentage of SIDS deaths by month in England and Wales, again in the 6 years before the intervention campaign [167, 168].

Figure 1.3 Seasonal distribution of SIDS infants in England & Wales 1985-90



Source : OPCS health and population monitor [167, 168]

Clearly, over this 6 year period there was an excess of deaths in the winter months. Of the previous studies, 19 reported death by month (*6, 7, 8, 10, 11, 12, 16, 19, 22, 26, 29, 30, 36, 37, 44, 48,49, 59, 64*). All reported a similar seasonal distribution with the exception of Ponsonby (*59*) in Tasmania who noted a lack of winter predominance in the final year of her study in 1991. Wagner's study (*22*) in France showed a similar seasonal distribution amongst other sudden unexplained deaths not diagnosed as SIDS, due, in part, to deaths from infections which predominate in the colder months. There was no such distribution amongst other neonatal deaths (*8, 16*).

Seasonality could be having an effect on SIDS rates through multiple associated risk factors, namely infectious agents, ambient temperature, nutritional or metabolic processes, infant care practices, or other behavioural or life-style factors. Three studies (*43, 44, 54*) have examined SIDS incidence and outdoor weather temperatures. A correlation was found between incidence and low minimum temperature 4 to 6 days earlier perhaps suggesting that parents may overcompensate for cold weather by using too many covers and not removing the covers as the outside temperature increases. Several studies (*7, 26, 30, 48, 59, 64*) have shown that the seasonal distribution was far more marked in infants aged over 12 weeks than those younger, although not all studies have agreed with the particular finding of an interaction between postnatal age and season of death (*16, 29*) . Fedrick (*7*) and Ponsonby (*59*) also showed an excess of males in winter whilst a study in England and Wales by Buvé (*37*) in 1986 suggested the winter increase in SIDS was more marked in the higher social classes but this did not reach statistical significance.

Gender

Of the 45 studies that reported infant gender, 43 showed a predominance of male infants within the SIDS group, ranging from 55% to 73%. The univariable difference was usually significant unless there was also a higher proportion of males in the control group. One study in Sheffield by Knowledon (*18*) showed no difference amongst 50 SIDS infants and one study in Hong Kong (*39*) contained more female infants in the SIDS group, although this may be due to small numbers (12 girls and 9 boys) rather than any ethnic difference. The overall mean proportion of males from the 45 studies was 61.2%. Bartholomew's study (*42*) in Scotland showed a similar male preponderance amongst other infant deaths. Studies by Kraus (*2*) in Californian and Irwin (*69*) in Washington State showed no gender difference in native American infants, whilst a New Zealand study conducted by Borman (*65*) showed no gender difference in the Aboriginal population. Kraus further showed no difference in gender amongst the black population of California but Hoffman's multi-centre study (*21*) in the United States showed a predominance of black male infants (60%).

Birthweight

For 10 studies birthweight was used as a matching factor. A further 40 studies reported birthweight statistics, in 36 of these studies the SIDS infants had a significantly lower birthweight compared to the control group. In 3 studies (*10, 39, 45*) the results were in the same direction but not significant. The number of SIDS in these studies were small and for the latter two there was a very low response rate suggesting a possible underestimate of low birthweight if the non-responders were mainly from the lower socio-economic groups where birthweight is generally lower. Bartholomew (*42*) demonstrated no significant difference in birthweight between SIDS infants and other infant deaths.

Gestation

For 4 studies gestational age was used as a matching factor. A further 31 studies reported statistics for gestational age, in 27 studies the SIDS infants had a significantly shorter gestational age compared to the control group, in 2 studies (*2, 39*) the results were in the same direction but not significant. Bartholomew (*42*) demonstrated in her study that other infant deaths had a similar pre-term disposition. Interestingly, one study carried out by Karagas (*34*) in Washington State showed *no significant difference* in pre-term age but more SIDS infants delivered post-term (> 41 weeks). This was significant for those whose births were induced but not augmented. Many studies treated delivery after 37 weeks as an ideal reference group for gestational age and therefore did not give details on post-term infants. Of the few studies that measured late gestational age, Steele (*4*) found post-term delivery to be significant. A slight excess of post-term SIDS infants was noted by Protestos (*5*) and Kilkenny (*70*) but Kraus's early multi-centre (*2*) study in the United States showed similar proportions of post-term infants in the index and control groups.

Maternal age

For 6 studies maternal age was used as a matching factor. A further 40 studies reported a comparison of maternal age of which 35 studies found SIDS mothers to be significantly younger than control mothers. In 3 small studies (*10, 23, 39*) the difference was in the same direction but not significant. Bartholomew's study (*42*) suggested young maternal age could also be a factor in other infant deaths. In only one study (*22*) was maternal age not found to be significant, and even in this study no univariable statistics were available, maternal age was stated to be non-significant when corrected for parity.

Marital Status

Marital status was reported in 28 previous studies. In 3 studies marital status was a matching factor (*7, 12, 37*), in 19 studies (*3, 8, 16, 21, 26, 29, 30, 35, 43, 44, 49, 55, 57, 58, 65, 67, 69, 70, 74*) single parenthood was a significant univariable factor, while in 3 studies (*2, 5, 23*) the results were not significant but in the same direction, in 1 study (*24*) the direction of the result was not reported. Only 2 studies did not find a difference in marital status between the SIDS and control parents; in the US study conducted by Schoendorf (*46, 47*) the results were only quoted as multivariable statistics and in Lee's study in Hong Kong (*39*) all the mothers in both groups were married, which may reflect cultural norms rather than any characteristic associated with SIDS.

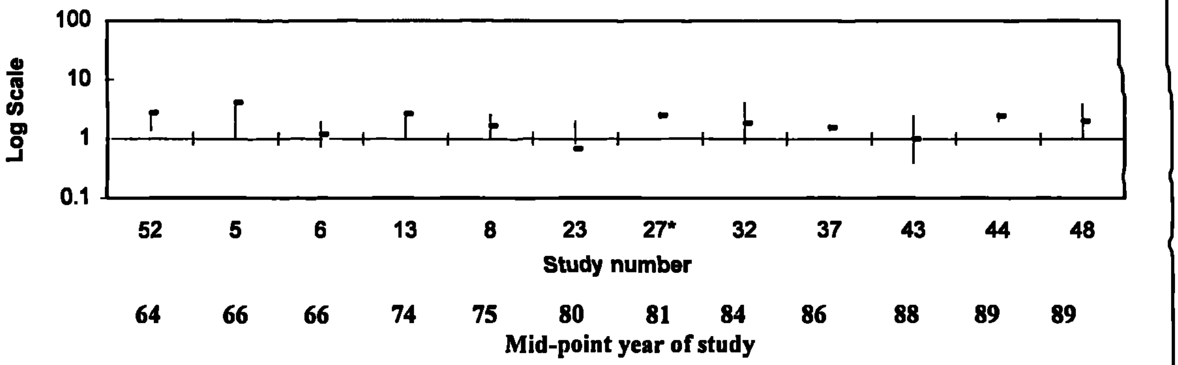
Number of children

Many studies have found SIDS families to be larger compared to the control population. Differences in either the number of children or parity were reported in 37 studies. Parity was used as a matching factor in 6 studies (*4, 7, 9, 12, 56, 66*), in 24 studies (*2, 5, 8, 13, 15, 19, 21, 26, 35, 42, 43, 44, 45, 54, 55, 57, 58, 59, 60, 65, 67, 69, 70, 74*) the findings showed SIDS families to be significantly larger, in 4 studies the results were in the same direction but not significant (*23, 32, 48, 52*) and in 2 studies the direction was not reported (*22, 30*). Only one very small study, conducted by Lee in Hong Kong (*39*) showed no difference in parity.

Socio-economic status

Socio-economic status was measured in several different ways. It was difficult to find a summary measure that was consistent amongst the studies. Figure 1.4 presents a loosely defined dichotomous measure comparing those families with unskilled occupations or no employment with those in semi-skilled, skilled and professional employment. The findings are represented by the univariable odds ratios for each study along with vertical lines that represent the 95% confidence interval, longer lines suggesting that small numbers were studied because of the wide intervals. These have been plotted on a logarithmic scale on the y axis. The x axis shows the different studies, arranged in ascending order according to the mid-point year of study with the earliest studies first.

Figure 1.4 - Socio-economic status : OR & 95% CI from previous studies



* SIDS and controls aged > 13 weeks

Of the 12 studies, 7 demonstrated that significantly more of the SIDS parents were in an unskilled occupation or were unemployed, the remaining 5 showed no significant differences although 3 were in the same direction. Excluding the one cohort study (*52*), the one case-control study (*37*) that used a control cohort and the one study (*13*) that did not publish the necessary data, the pooled summary estimate was significant (OR=1.75 [95% CI : 1.52 to 2.02]). The case-weighted summary estimate for all the studies where data was available was also significant (OR=1.80 [95% CI : 1.12 to 2.58]). A consistent difference has been demonstrated over time although the univariable risk associated with low-socio-economic status was not very high when combined across studies.

The whole question of socio-economic status and its association with SIDS is very difficult to measure. One can attempt by proxy to stratify families into different social groupings using income, education or employment but the diversity of the individual and the circumstances surrounding that individual can lead to false assumptions and misclassification. Even if we do achieve some suitable proxy measure we are still none the wiser as to what this means. Many studies have shown, using the measures mentioned above, that a greater proportion of SIDS families have lower socio-economic status. Is SIDS therefore associated with poverty? Disruptive family routines? Avoidance of public health messages? Or is the socio-economic measure masking some other associated factor such as illness, failure to thrive, exposure to tobacco smoke etc. Perhaps the different social strata mark out different types of infant death with different epidemiological characteristics and different risk factors. The CESDI SUDI study looked at several socio-economic markers and associated factors to address this problem.

Other epidemiological features

There are several other epidemiological features, investigated by previous studies, that are still open to interpretation and further study.

For instance, there is a suggestion of a temporal sequence of events characteristic of SIDS infants. Bergman in Washington State (*10*) showed that 74% of deaths were discovered between 6am and noon, 16% between noon and 6pm and only 10% between 6pm and 6am. Froggatt (*6*), using different cut-off points, showed that 50% were discovered between 12pm and 8am, 36% between 8am and 4pm and 14 % between 4pm and 12pm. The majority of deaths appear to have been discovered after the night-time sleep. Golding (*12*) however, reports the findings of a study conducted on behalf of the Foundation for the Study of Infant Death in the UK in 1980-81 and sheds more light on the sequence of events. She reports that 43.1% of deaths occurred between midnight and first being seen in the morning and 50.7% between being seen in the morning and 9pm. A further 6.2% of the SIDS infants died in the evening between 9pm and midnight. This suggests an equal proportion of SIDS infants died during the night and after being seen to be alive in the early morning.

Four studies looked at the day of the week that the death occurred. Rintahaka in Finland (*8*) found significantly more deaths occurred at the weekend, suggesting that disruption of routine care was a possible factor. In Froggatt's study (*6*) the peak incidence was also on a Sunday, although this did not reach significance. However, Fedrick (*7*) and

McGlashan (*29*) both found that the peak incidence occurred on a Thursday, in the latter study this was significant.

Many studies (*2,5,8,12,13,16,26,32,54,57,59,70*) have found a higher incidence of SIDS amongst twins and triplets. Although this is significant, the numbers are too small in any one study to conduct any meaningful analysis. Kahn (*20*) specifically compared sibling history of twin infants, one of whom died of SIDS. The twin that died had a significantly lower birthweight and shorter height than the corresponding sibling and both greater episodes of cyanosis or pallor and repeated episodes of profuse sweating observed during usual sleep.

Six of the epidemiological studies have looked at previous infant deaths, 3 have found the prevalence higher amongst SIDS families (*13, 21, 42*) and 3 have not (*8,23,52*). Only one of these studies (*21*) mentioned previous SIDS deaths which occurred significantly more amongst SIDS families, suggesting a possible genetic effect. Golding (*12*) reports of other studies that have looked at recurrence risk and calculates the univariable risk of a further SIDS is increased by a factor of 10, although this factor reduces to approximately 3 when account is taken of the social and maternal background.

Chapter 5

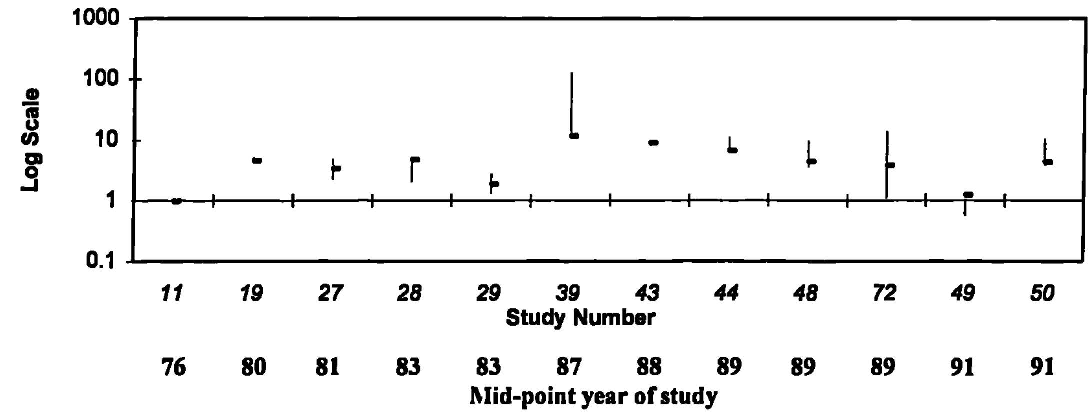
Risk factors before the fall in incidence

<u>Sleeping position</u>

The association between prone-sleeping position and SIDS noted by Abramson in the 1940's [16] was again investigated by Bergman [66] in Washington State in the 1960's. He found no difference in sleeping position at the time of death. The reason for this was revealed when he conducted a rather impromptu survey of usual sleeping position amongst 214 parents in 'both private and clinical offices'. The survey revealed that prone-sleeping was by far the most common position for infants at that time, less than 10% sleeping supine. It wasn't until a decade later that the association of sleeping position and SIDS was again reported.

Figure 1.5 shows the findings of the 12 studies from 1976 to 1991. The risk relating to position put down for the last sleep was taken if available but for most studies either the usual position or no indication were given. For 7 studies (*27, 28, 29, 39, 43, 48, 72, 50*) the reference group was taken as both the lateral and supine position rather than just supine as either no distinction was made or the numbers were too small.

Figure 1.5 - Prone position : OR & 95% CI from previous studies

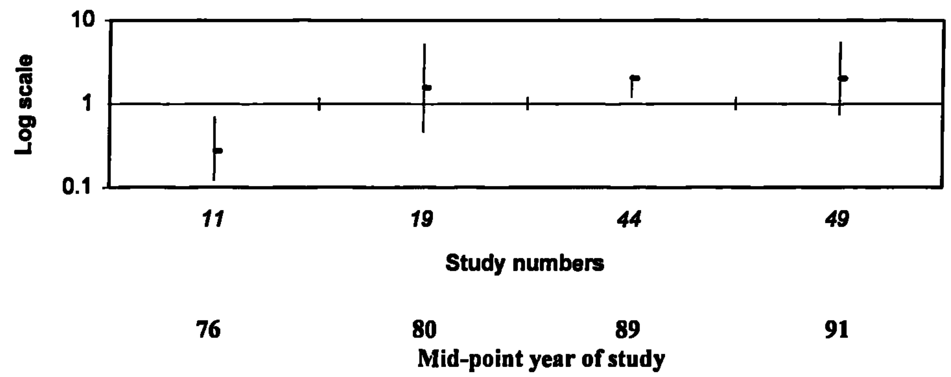


One study (*19*) used near-miss SIDS infants as controls, one study had a cohort design (*72*) and one study used a retrospective cohort of observations (*11*). In this latter study, the prone-sleep position was not significant when compared with supine as so few infants adopted this position, however, using side as well as supine in the reference group yielded a significant result (OR=3.08 [95% CI: 1.97 to 4.82]).

The general picture from these studies suggests that prone-sleeping position was a consistent risk factor amongst SIDS infants. Findings from only two studies (*11, 49*) did not reach significance, in both studies very few SIDS or control infants were put down in the supine position. The pooled summary estimate for the 10 case-control studies was significant (OR=2.84 [95% CI : 2.40 to 3.37]), as was the weighted summary estimate for all 12 studies (OR=3.27 [95% CI: 1.77 to 6.55]).

Only 4 studies looked at the possible risk association with the lateral-sleeping position and SIDS (supine position was used as the reference group). Figure 1.6 shows no overall pattern.

Figure 1.6 - Lateral position : OR & 95% CI from previous studies



Tonkin's study (*11*) showed side-sleeping to be significantly protective whilst Mitchell's study (*44*), again in New Zealand many years later, suggested side-sleeping to be a small but significant risk factor, although this became non-significant in the multivariable analysis. The difference in results may be explained by the reduction in prone-sleeping which began in New Zealand towards the end of Mitchell's study following an intervention campaign. The two other studies by Kahn (*19*) who used near-miss infants as a control group and Klonoff-Cohen (*49*) showed no significant differences in the univariable analysis although the direction of both findings were towards a risk effect rather than a protective one. The pooled summary estimate for the three case-control studies (*19, 44, 49*) that did not use a large control population was not significant (OR=1.27 [95% CI : 0.87 to 1.86]), nor was the weighted summary estimate for all four studies (OR=1.41 [95% CI : 0.68 to 3.01]).

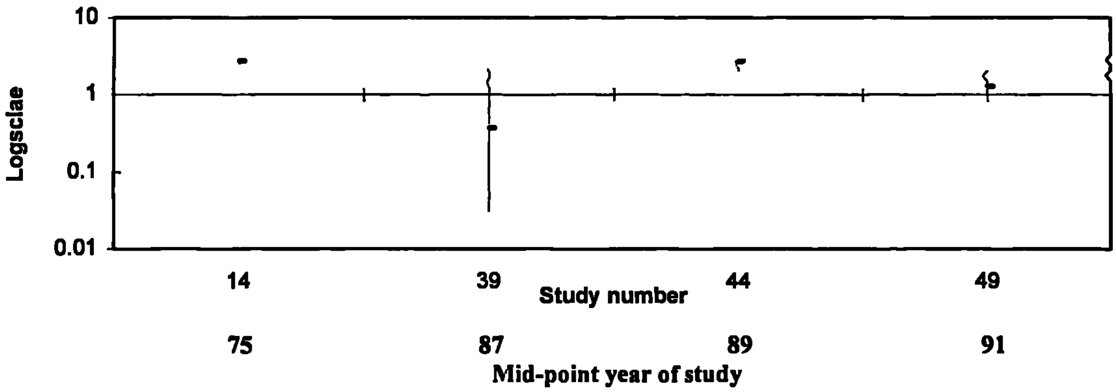
Thermal stress

Only 5 studies have looked at the problem of thermal stress. McGlashan's study (*29*) in Tasmania noted that significantly more SIDS families heated their homes less whilst Klonoff-Cohen (*49*) found no significant differences in the type of heating used. However, Gormally (*45*) in Ireland found that 39% of the SIDS infants were warm to the touch when discovered and 15% were described by the *parents* as 'sweaty'. Two studies addressed the issue more thoroughly, measuring thermal resistance (tog value) of bedding and clothing used during the infant's sleep. Both Fleming's study (*43*) in Avon and Ponsonby's study (*48*) in Tasmania found the SIDS infants to be more heavily wrapped than the controls, both usually and for the last sleep, a median difference of approximately 1 tog unit. Calculating the difference per additional tog value above 8 togs, both studies demonstrated SIDS infants to be wrapped significantly warmer.

Bed-sharing

Only 4 previous studies have looked at bed-sharing with the parents as a risk factor. The findings are shown in Figure 1.7.

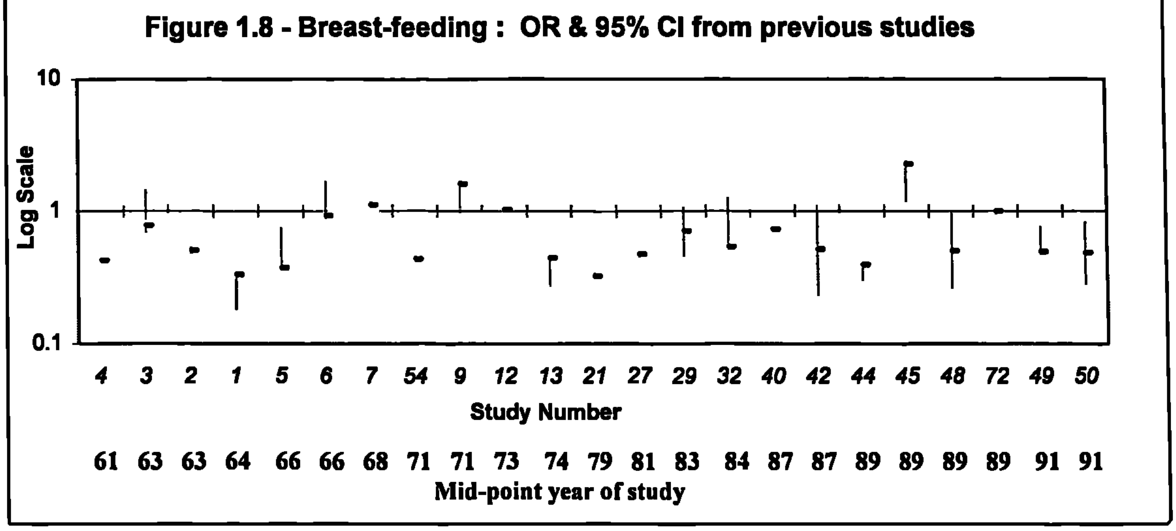
Figure 1.7 - Bed-sharing: OR & 95% CI from previous studies



Only 2 of the studies (*14, 44*) looked at bed-sharing for the last sleep, one of these (14) used usual practice for the controls, both found bed-sharing to be a significant risk factor. The pooled estimate for these two studies was significant (OR=3.13 [95% CI : 2.42 to 4.04]), as was the weighted estimate (OR=2.41 [95% CI : 1.89 to 3.89]). The other two studies (*39, 49*) looked at the usual practice of bed-sharing. The pooled estimate for these two studies was not significant (OR=1.13 [95% CI : 0.73 to 1.75]), nor was the weighted estimate (OR=1.17 [95% CI : 0.63 to 2.04]).

Breast-feeding

Breast-feeding has been investigated by 23 studies as a possible protective factor associated with SIDS. Few studies looked at duration of breast-feeding and of those that did, different time-intervals were used. For this analysis the intention to breast-feed, regardless of duration, was chosen, to incorporate as many studies as possible.

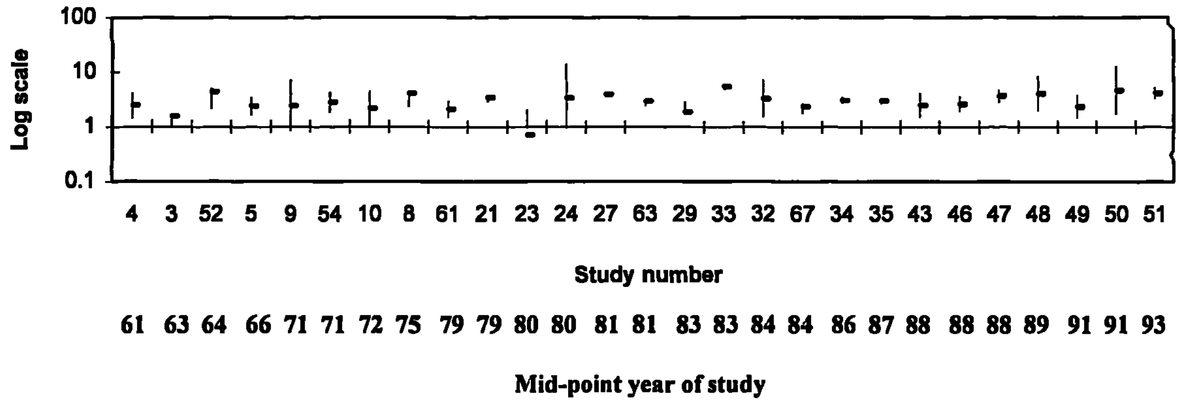


The general impression suggests an overall univariable protective effect from breast-feeding, 11 studies showed a significant protective effect and a further 7 studies were in the same direction but not with sufficient strength. Of the 23 studies, 3 did not provide the necessary data (*2, 21, 27*) and 2 were cohort studies (*54, 72*), the pooled summary estimate for the remaining studies was significant (OR=0.59 [95% CI : 0.54 to 0.65]), the weighted estimate for all the studies just remained significant (OR=0.60 [95% CI : 0.36 to 0.99]). One study, conducted by Gormally (*45*) in Ireland showed breast-feeding to be a significant risk factor, however this finding may be flawed as control infants were only considered to be breast-fed if feeding continued up to the first 6 weeks whereas with the SIDS infants this was either up to the first 6 weeks or up to when the baby died. Some of the studies however, suggested that the lower frequency of breast-feeding amongst SIDS infants was ascribed to various other factors known to be associated with SIDS. When factors such as young maternal age, employment status and maternal smoking were added in those studies that conducted a multivariable analysis, breast-feeding became non-significant. A few studies also looked at age of introduction to solids, number of feeds a day and the effect of breast-feeding and pre-term infants but found no significant differences. There may therefore be a protective effect from breast-feeding although the association may be a weak one.

Exposure to tobacco smoke

Maternal smoking was reported in 27 studies (in some it was not stated whether this was during pregnancy or after pregnancy). The results are presented in Figure 1.9.

Figure 1.9 - Maternal smoking : *OR & 95% CI from previous studies*



The univariable risk associated with maternal smoking has been confirmed by nearly every study that has investigated this factor. Of the 27 studies, 24 reported a significant effect and 2 (*9, 24*) were in the same direction but not of sufficient strength. Only one study (*23*) from Ireland was in the opposite direction which may be due to the low numbers ascertained. The pooled summary estimate, excluding 4 cohort studies (*52, 54, 63, 67*) and one case series (*61*), was significant (OR=3.34 [95% CI : 3.13 to 3.57]), as was the weighted summary estimate for all of the studies (OR=2.95 [95% CI : 2.16 to 4.03]).

Paternal smoking was reported in 9 studies. Six of these (*18, 27, 29, 44, 49, 51*) showed paternal smoking to be significant as a univariable factor, three studies did not (*6, 10, 39*). The recent study by Mitchell (*44*) in New Zealand reported that the risk of paternal smoking became non-significant when adjusted for other factors.

Other risk factors

More than 140 further different risk factors have been investigated by previous studies. These can be split into four main areas, namely; factors prior to or relating to pregnancy; factors relating to labour or delivery; factors relating to the neonatal period; and postnatal factors. A list of these factors and whether the univariable results achieved significance is set out in tabular format in Appendix II. Some of the more common findings amongst the SIDS mothers included the short time between pregnancies, late or non-attendance at pre-natal classes and vaginal or urinary infection during pregnancy. Some of the more common findings amongst the SIDS infants included the greater number admitted to Special Care Baby Units and recent illness prior to death.

Looking at these tables, one is immediately struck by the discrepancy between studies regarding the significance of many of the factors. Where more than one study has investigated a particular factor there are only 20 variables (20.2%) where there is a consensus of agreement. However, these tables serve only as a guide for future investigations and do not indicate the strength and directions of the findings. The lack of significance may be partly due to the way factors were defined and measured in different studies, partly due to the variation in the number of infants studied and because some studies have only quoted multivariable statistics which are usually less significant when controlling for other variables. The tables in Appendix II should serve as a useful template for further meta-analyses.

Chapter 6

Design of the CESDI SUDI study

Study objectives

The Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) was set up in the UK in 1992 after concern was expressed by the Parliamentary Select Committee about the high infant mortality rate. As part of that enquiry a two year case-control study was initiated in February 1993 to investigate all sudden unexpected deaths in infancy (SUDI). The deaths included all infants from one week to one year old who died suddenly and unexpectedly. The vast majority of these deaths would be SIDS but also included infants who died from an apparently non-life-threatening acute illness, from an unrecognised pre-existing condition or from accidental or other traumatic death. The inclusion of a wider range of unexpected deaths was thought important because it is often not possible to distinguish between SIDS and other unexpected deaths until the full post-mortem results are available. The details of the inclusion criteria are set out in Appendix III.

The study began one year after the national intervention campaign to reduce the risk of SIDS. The main objective of the study was to assess the changes in risk factors previously identified before the national campaign and new associations that may have emerged, in particular to investigate those factors that might be avoidable or amenable to change.

Geographical area

Funded by the Department of Health, the study began in two of the former health regions, South Western and Yorkshire on 1st February 1993 and a third health region, Trent, from the 1st September 1993. These three regions had a population of just under 12 million. Over the two years the expected number of births was 350, 000. With the anticipated number of SIDS deaths being much lower than in previous studies, the geographical area covered was vast, making this study the largest population-based case-control investigation of SIDS ever conducted in Europe.

Case notification

A communication network, involving multiple groups of health professionals and lay organisations was established in each of the participating regions before the study began (see Appendix IV). This was to ensure that all sudden deaths of infants were promptly notified to the co-ordinating office. Slower notification routes were used to check complete ascertainment of cases, including returns to the district registrar and death registration information collected by the OPCS. The aim was for all such deaths to be reported to the relevant office within 24 hours. On receipt of the notification, immediate contact was made with the family's health visitor or general practitioner. A brief interview was arranged with the family as soon as possible to talk about the events immediately surrounding the death, the aim being to see the family within 5 days. Far from being intrusive, experience from previous studies carried out in Avon showed that families welcomed the early intervention. The study researchers were all qualified health visitors and midwives who could offer both early bereavement support to the families and professional support to the family practitioner or health visitor. At the initial visit to the index family, the researcher obtained informed consent to take part in the study, and then took a standardised, semi-structured history, including a narrative account of all events within the last few days, and in particular the events surrounding the infant's last sleep period. The researcher made a second visit to the index family a few days later (within 2 weeks of the death), to complete the full questionnaire.

Control selcction

Four control families were selected for each case. Given the number of cases expected over the two years, this was the optimum number of controls required to maximise the power of the study. The control infants were taken from the caseload list of the health visitor of the index family. The control families were identified as the two families with babies next older than the index baby, and the two families with babies next younger. If four infants could not be chosen from the list of the index family's health visitor, the caseload list of a health visitor working in the same or a nearby practice was used. If the family's health visitor felt that there was a strong reason (e.g. psychiatric illness in the parents, recent bereavement etc) for not including a particular control family, the next family was chosen, but a note was made of the reason for the exclusion. If the contact could not be made with a chosen control family after three attempts by the researcher, or if the family were away (e.g. on holiday), or if the family declined to take part in the study, the next family was chosen, and a note made of the reason for the substitution. The control families were interviewed as soon as possible, the aim being within 2 weeks of the death, so that the external environmental factors (e.g. outdoor temperature, local community infections etc) were comparable between the two groups.

Unlike the index families, the control families were only visited once. The same questionnaire was used. A precisely similar narrative account was obtained, with a particular emphasis on the comparable sleep period: the "reference sleep". The "reference sleep" was identified by the researcher as the sleep period of the control baby in the 24 hours before the interview closest in time of day or night to the index baby's last sleep. Particular importance was attached to whether the index baby died during what the parents identified as a night-time sleep (i.e. the baby was in night-time bedding, clothing and place) or a day-time sleep (i.e. the baby was in bedding, clothing, and place seen by parents as appropriate for day-time sleeps). The "reference sleep" was matched by the parents' perceptions as a "day-time" or "night-time" sleep as appropriate.

Data collected

The questionnaire contained information on socio-demographic factors, medical history of the baby and other members of the family, detailed information on the family structure, information on recent illness of the baby and other family members, a full narrative account of the events in the 24 hours before the death or interview, and very detailed information on the circumstances, timing, events, sleeping position, bedding heating, and other environmental factors at the time of the last sleep or the equivalent sleep in the controls. The database from the questionnaire contained over 600 fields. All medical, nursing, and midwifery records relating to the mother and the baby were examined and transcribed.

A full, paediatric necropsy was performed to an agreed, standardised protocol, on all babies in the study.

Classification of death

Each of the deaths were reviewed by a regional confidential review panel. This was a multidisciplinary committee consisting of representatives of each of the professional groups involved in the care of mothers and young children. Each committee thus included an obstetrician, a general practitioner, a hospital paediatrician, a midwife, a health visitor, a community paediatrician, a paediatric pathologist, a general pathologist, and a chairman, who was usually a specialist in public health medicine. At the meeting, all factors which may have contributed to the death including the circumstances of the death, the history, any relevant social factors, the gross pathology, histopathology, microbiology, and the biochemistry were reviewed, and the cause of the death was derived using the *Avon classification system* [113]. The *Avon classification system* includes information on clinical, social and pathological findings, which are each awarded a score of I (no significant findings), II (findings which were probably of significance, but were not sufficient to fully explain the death), or III (findings which provided a full and sufficient cause for the death). The overall classification of the death is then decided by the highest numerical score given to any of the findings. Deaths classified as I or II are thus considered to meet the strict definition of SIDS, whilst those classified as III are considered to be fully explained SUDI. The cause of death agreed at this meeting was taken as the final classification of the death.

Chapter 7

Dealing with aspects of bias and data quality

There are several aspects of bias relevant to any case-control study. As far as possible these aspects were dealt with in the design of the study.

Selection bias

Ideally the selection of controls should be carried out on a randomised basis to both prevent unintentional matching and provide results that could be generalised to the whole population. The method of selection of controls in this study, using caseload listings of the index health visitor, is based on a similar method to that previously used in the *Avon Infant Mortality Study* (AIMS) [27]. This selection method is not randomised. The control infants are selected from the caseload listing by matching for the age of the index infant, the control families are thus partially geographically matched by using the health visitor caseload which covers a particular area of the community. However, this method of selection of controls was chosen as a result of a comparison of approaches to control selection carried out in a previous study in Avon [138]. In this previous study, a comparison was made between the controls selected as outlined above with those who were obtained by random selection, choosing every 125th baby on the Avon birth register. This showed that, whilst the latter method initially selected a group of controls who were more representative of the socio-economic mixture in the overall community, the rate of refusals, particularly amongst the more deprived sections of the population, was so high that the controls actually obtained represented a group skewed away from that most deprived part of the population. Previous findings suggest that many of the SIDS families come from the lower socio-economic group. Using the randomised method, the socio-economic differences between the cases and controls would therefore be over-emphasised. Conversely, choosing controls from the index family's health visitor where both groups come from the same area, the socio-economic differences between the cases and controls would be under-emphasised. Neither selection process is perfect but if one wants to establish any true difference in socio-economic status between the two groups one must run the risk of under-emphasising that difference. For this reason, the selection of controls was decided as set out above. This approach to selection of controls also facilitated rapid contact with the control families.

Classification bias

Classification of SIDS by post-mortem is unreliable, dependent on the variation between the judgement and knowledge of each pathologist. In an attempt to achieve consistency of judgement a review committee of medical experts was utilised provided with all the available information including the post mortem report, hospital records and information collected from the study questionnaire. To avoid the risk of certain individuals involved in any case biasing the outcome by their direct knowledge or views, the records were anonymised and committees were constituted in such a way as to ensure that no member of the Committee came from the district in which the death had occurred.

As part of the confidential enquiry process, an independent study was conducted to assess the regional panels in terms of the comparability of their findings and an audit of this type of classification process. This involved three panels, one from each region, reviewing the same six cases, each sitting was both tape-recorded and observed and both panel decisions and comments from their members were collected. The study found a large variation in the way the panels were organised and the amount of information available for each case. The chairmen exerted considerable influence, and different chairmen exerted a variety of biases on the discussion. Consequently the classification regarding the SUDI deaths was not consistent. The *Avon classification system* used for the CESDI SUDI study fared better than the alternative *Sheffield classification system* (62% agreement vs 35% agreement) but even with these six cases there was one case classified as an explained death by one panel and a SIDS by the other two panels. The results of this study were only available after the two year dataset had been collected, but as review panels are a relatively new concept the incompatibility between panels was anticipated before the CESDI SUDI study began. For those cases who were borderline SIDS or fully-explained deaths the elected consultant paediatrician in each region made the final decision, sometimes in consultation with the paediatricians from the other two regions. In an attempt to achieve consistency of classification the review panels perhaps highlighted the difficulties pathologists have in determining when an infant death can be classified as SIDS.

Recall bias

Specific questions relating to circumstances around the time of death or reference sleep may be difficult for the parents to answer if not asked soon after the event. Recall bias was therefore minimised by attempting to see the index families as soon as possible after the death. At this initial interview the index parents were asked to describe the events in the 24 hours leading up to the death and although the questionnaire was not formally filled in at this stage, the relevant information required was prompted for in the narrative account. The reference sleep for the control infants was chosen in the 24 hours immediately prior to interview, again to reduce recall bias. A similar narrative account was taken from the control parents of their routine leading up to this sleep.

Interviewer bias

Four research interviewers were recruited in each region. To ensure consistency in approach, wording and understanding of each of the questions prior to the start of the study, several steps were taken. All researchers were chosen from a common background of midwifery or health visiting. The interviewers were involved in the design and wording of the questions in the questionnaire. Three full day joint training sessions were held for the researchers, and all participated in "dummy" interviews with volunteer families. A set of guidelines was developed and regularly updated to deal with specific questions, with particular reference to the conduct of the interviews and any ambiguities in the questionnaire. Further meetings to discuss and ensure consistency of the questionnaire were held at three monthly intervals throughout the study.

Data quality

The data collected by the researchers was also entered by them into a database created using SPSS Data Entry II [169]. Using the same researchers to both collect and record the information meant that specific queries could be dealt with quickly and accurately. All records were subject to careful checking to ensure accurate recording of the information collected. The details of this are given in Appendix V.

Reliability of information

What one cannot do is check the accuracy of the information given by the parents. In some studies repeated questions can be inbuilt into the questionnaire to cross-check for compatibility of the response. With interviewing recently bereaved parents, it was not an option to burden parents with extra questions of this nature. Cross-checking was only done with information given by the parents that could also be found in the hospital records, the parental information was used if there was a discrepancy. As long as the parent understood the question, the interviewer was allowed no interpretation of the parental response, even if it was considered wrong. Accuracy was therefore compromised but consistency was maintained.

Part II

Analytical design, ascertainment and the univariable results

Chapter 8

Analytical Design

Main hypotheses to be tested

A structured analysis was included in the initial design of the study to avoid trawling the results once the data were collected. The hypotheses to be tested fell into 15 main areas, each with several factors or interactions that needed addressing:

(i) Sleeping position
(ii) Thermal environment
(iii) Smoking
(iv) Recent illness in baby
(v) Bed-sharing and room-sharing
(vi) Dummy use
(vii) Breast-feeding
(viii) Infant mattress
(ix) Alcohol and illegal substance use
(x) Length of time baby was left unattended
(xi) Apparent life-threatening event
(xii) Maternal depression
(xiii) Previous hospital admissions or attendances
(xiv) Previous deaths and access in emergency
(xv) Recent major life events

A list of the specific variables associated with each area is given in Appendix VI. Most of these hypotheses were based on *a priori* knowledge. Several previous studies, before the intervention campaign, suggest some of these risk factors to be strongly associated with SIDS, whilst the evidence for other factors lacks sufficient clarity. Given the reduction in the number of deaths certain questions needed to be answered. How important now are factors addressed in the "Back to sleep" campaign such as prone-sleeping position, thermal environment and infant exposure to tobacco smoke? The side-sleeping position was recommended as an alternative to the prone position but how safe is it? Does breast-feeding have a protective effect or is it just a life-style marker? An excess of SIDS families are from the more deprived sections of the community associated with many adverse factors, such as poor housing, insecure tenure, higher levels of alcohol consumption and tobacco use, more drug abuse and other disruptive factors. How does this affect the infant and the parental routine? If SIDS occurs in normally healthy infants, how normal and how healthy are these infants? Previous studies suggest bed-sharing is a strong risk factor yet several countries where bed-sharing is the norm continue to have very low SIDS rates. What is it specifically about bed-sharing that yields an associated risk for SIDS infants and which group of families does this apply to? The apparent protective effect of dummy use has only been found in one previous study, in New Zealand, and needs further clarification. The recently publicised hypothesis relating to infant mattresses has not been investigated in any previous case-control study. The hypothesis is that under certain conditions, fungal growth on PVC covered cot mattresses may lead, under certain conditions, to the generation of highly toxic gases from antimony trioxide. Because this hypothesis has caused much concern to parents and health professionals, results from the first year of this study have already been published [170]. This analysis will look at the data from the two years.

Each of the factors listed in Appendix VI were investigated in the univariable analysis. Continuous variables were plotted and dose-response relationships calculated where appropriate. The data obtained in this study was complex; many factors were related to each other (eg smoking was associated with socio-economic deprivation). The risks associated with each factor in the univariable analysis may not reflect the actual risk in reality. Many of the factors described are inter-dependent and it is only when we analyse these factors together that a more accurate picture can be ascertained. A two-factor stratification will give us some idea of the relationship between two variables but the interpretation gets complicated when further variables are added. In order to understand these complex interactions, in which the variations in several factors need to be studied simultaneously, the techniques of multivariable analysis must be used.

Multivariable modelling

The models used in this analysis were based on a single dependent outcome variable (whether the infant was a case or control) and two or more explanatory predictor variables. The risk associated with each predictor variable was calculated using *conditional multiple logistic regression*. This technique stems from basic linear *regression* where the value of one variable can be predicted from the value of the other. The outcome variable was binary, hence the term *logistic*, and as there were several predictor variables the regression analysis was termed *multiple* logistic regression. The data in this study were also matched in that control infants were matched as closely as possible to the same age of the index infants. The regression was therefore *conditional* on the matching, the age distribution was taken into account for each model and the results were conditional on the fact that the two groups were of similar age.

Multivariable entry criteria

To choose which variables were allowed in the multivariable model, entry criteria needed to be adopted before the analysis began. The variables to be tested were chosen using the following criteria :

(i) The variable must directly relate to one of the 15 primary hypotheses or epidemiological characteristics set out before the study began.

(ii) In the univariable analysis the variable must have achieved statistical significance ($p<0.05$). Significance levels are usually set more generous than this ($p<0.10$, $p<0.15$ or $p<0.20$) as the risk or protective effect of some univariable factors actually increase when other variables are added to the model. However, for this study, with so many variables being investigated, a strict criterion was set to reduce the possibility of false-positive findings.

(iii) If more than 5% of values were missing, the variable was initially treated separately from the modelling process. Although many variables had only one or two values missing, this became a cumulative effect when many variables were added to the model. Those variables with many values missing were therefore excluded from this earlier process and tested later once the best fitting models were finalised.

(iv) For some variables it was difficult to identify which of the many possible indicators were the most appropriate to use. For instance, there were several indicators for socio-economic deprivation, some of which may be so closely correlated that one proxy measure would be sufficient for the analysis. For these variables an initial investigation was conducted before the modelling process began.

The variables were of three types; continuous, dichotomous and multi-categorical. For the last, dummy variables were constructed comparing each category with a reference group.

Model selection and construction

There are four main approaches to automatic selection procedures, none of which provide infallible tactics in producing predictor variables. The forward procedure begins with a null model and adds each significant variable until the addition of a further variable is (in some sense) insignificant, the disadvantage being that variables included in the final model may have only been significant in the early stages of the procedure. The backward procedure is similar but starts with a full model and eliminates the least significant, the disadvantage being that variables may be eliminated at an early stage but may have proved significant in the later stages. The stepwise procedure overcomes both these disadvantages by using the forward procedure but allowing elimination as in the backward procedure. Finally there is the best-subset selection procedure which calculates the best fitting model for any given number of predictor variables, although individual variables may not be significant. For this analysis the stepwise procedure was used. These procedures are a useful exploratory device but do not produce a definitive multivariable model that will answer all the hypotheses. For this we need to structure models using an intuitive approach with careful interpretation of variables that remain or fall out of the model.

With such a complex dataset it is important that the modelling process is based on some sort of logical structure. There are several approaches, each with their own advantages and disadvantages, three of which were adopted :

(i) A two-stage empirical model was constructed. Some variables describe the variation between the cases and controls but were not themselves amenable to change. These have been termed epidemiological characteristics. The initial construction first dealt with these variables after which the rest of the factors significant in the univariable analysis were added. There are difficulties with this two-stage empirical approach. Entering variables purely on the basis of univariable significance rather than using *a priori* knowledge of the factors and relationships between them, may produce an over-fitted model that is difficult to interpret. However, this approach will yield certain factors that are highly significant and need to be considered when constructing subsequent more specific models.

(ii) A temporal model was constructed building up the risks associated with SIDS over the sequence of events. Beginning with factors relating to the time of conception, then adding those relating to pregnancy, identifiable at birth, the post-natal factors and finally those factors relating to the circumstances just before the last/reference sleep . Again the resultant model may be over-fitted, but the importance of this approach lies in the significance of the factors relating to the different time periods.

(iii) Finally several smaller models were constructed containing the variable of interest, possible confounders and other variables that may not be directly related to the variable of interest but were highly significant in the previous multivariable analysis. These models overcome the problem of saturation and more accurately yielded the actual risk associated with different variables.

Statistical techniques

For both the univariable and multivariable analysis, the matching was taken into account using conditional logistic regression. This was carried out using the PHREG procedure in the SAS [171] package (results of this procedure have been verified against similar procedures available in SYSTAT, GLIM and EGRET). Odds ratios were quoted for categorical variables adjusted for the matching along with 95% confidence intervals, if an expected cell frequency was less than 5, the unadjusted Fisher's exact test was utilised. For multi-categorical variables, both odds ratios for each non-reference category and overall p-values were given. The significance of continuous variables were either quoted using the p-value or by multiplying the relevant parameters to reduce the number of categories within the variable to produce comparable odds ratios. In the multivariable models, single parameter testing was conducted using the Wald test, for more than one parameter, such as a multi-categorical variable, the Likelihood Ratio test was utilised. Both odds ratios and p-values were quoted for both those variables that remained significant in the resultant models and those that did not. For the latter, the estimates were calculated by adding the non-significant variable at the end of the modelling process. Any lack of fit in the model was tested using Martingale Residual plots. Stratification of variables were conducted by pooling results across strata using the Mantel-Haenszel test. Population attributable risks were calculated using the proportion of exposed in the index population divided by the multivariable risk associated with that factor [172]. For non-parametric distributions the median and interquartile ranges were used along with the one sample Kolmogorov-Smirnov goodness of fit test [173]. Centiles at birth were computed using Z-scores from the Fox-Pro Package [174].

Chapter 9

Ascertainment and quality of the data

Case ascertainment

There were 266 sudden and unexpected deaths in infancy identified during the period February 1st 1993 to January 31st 1995 in the three regions studied. Cross-reference with both OPCS and Registrar data in the Trent Region revealed 5 missed cases and probable under-reporting of deaths due to non-accidental injury. One case was missed in the South-West and no cases were missed in Yorkshire. The regional breakdown is given in Table 2.1.

Table 2.1 - Sudden unexpected deaths in infancy : regional breakdown of the numbers identified & interviews conducted

Region	All SUDI			SIDS			Explained SUDI		
	Identified	Interviewed		Identified	Interviewed		Identified	Interviewed	
		N	%		N	%		N	%
Yorkshire	108	106	98	84	82	98	24	24	100
Trent *	84	69	82	71	60	85	13	9	69
South-West	74	66	89	61	55	90	13	11	85
Total	266	241	91	216	197	91	50	44	88

** Started September 1st 1993*

Of the 266 sudden unexpected deaths, 216 (81.2%) were classified as SIDS by the regional review panels. Of these 216 SIDS cases, 19 families were not interviewed. In 3 cases a decision was taken not to interview because of police involvement and a concern (not subsequently confirmed) about possible non-accidental injury. In a further 4 cases the parents could not be traced (1 moved out of the region and 3 out of the country). Only 12 sets of parents of SIDS infants refused to take part in the study yielding a 94.3% consent rate. Epidemiological data available from public records (sex, place of birth, age of baby and parents, time of death, place of death, certified cause of death) was collected on all deaths.

For 3 SIDS cases no control families were interviewed. In 2 of these cases it was thought inappropriate to take controls as the family lived outside the region and the other case, which was also a refusal, was at the beginning of the study which was mistakenly thought not to require controls. The analysis therefore concerned 195 SIDS cases and their 780 matched controls.

Explained sudden unexpected deaths

From the post-mortems and other information available to the regional review panels, adequate explanation of the cause of death was identified in 50 cases. These causes are given in Table 2.2.

Table 2.2 - Sudden & unexpected cases with subsequent explained cause of death

Cause of death	Number	% of all deaths
*Infections**	18	6.8%
Accidental death	12	4.5%
Non-accidental injury	10	3.8%
Congenital abnormality	5	1.9%
Intussusception	2	0.8%
Metabolic disorder	1	0.4%
Necrotising entercolitis	1	0.4%
Bronchopulmonary dysplasia	1	0.4%

* Includes meningitis, rapid infection, bronchopneumonia & gastro-enteritis

The main analysis will concern the SIDS cases only.

Control ascertainment

As mentioned above, for 3 SIDS cases it was thought inappropriate at the time to take controls. The same decision was also made for 4 explained cases (2 accidental deaths, 1 non-accidental injury and 1 baby who lived out of the region). Four control families were therefore required for 259 of the cases. Of the 1036 controls required, 13 sets of control parents refused to take part in the study (1.3%), 21 control families were unable to be contacted after at least 2 attempts (2.0%) and 23 were thought not suitable by the family health visitor, mainly because of recent bereavement or illness (2.2%). For each of these control families a replacement family was immediately found yielding a 100% ascertainment of controls.

Time to first interview and matching

The time from the discovery of the death until the first interview of the index parents ranged from just a few hours to 94 days. The median time to the first interview was 4.5

days; 82% of families were interviewed within 14 days of the death, and 95% within 28 days.

Over two thirds of the controls were matched within 2 weeks of age to the index baby, over 90% within 1 month. The control infants were just over a week older than index infants, the median absolute difference was 9 days (interquartile range : 4 to 18 days). The reason for the discrepancy was because of the slight delay in contacting the control families and arranging the interview, age of control infants being taken at the time of interview. All univariable and multivariable analysis takes account of the discrepancy in age. The median time to control interview was less than 2 weeks from the death of the index infant.

Chapter 10

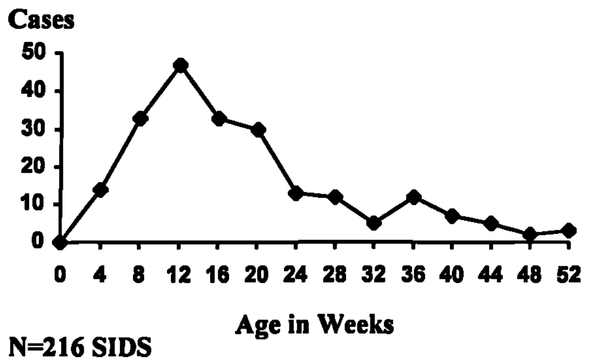
Main Epidemiological Features

The following epidemiological features concern the 216 SIDS cases. Age of infant was a matching factor whilst the other features were relevant to the deaths only and will therefore not be included in the multivariable analysis.

Age distribution

The age distribution of the cases can be seen in Figure 2.1, the median age was 14 weeks (interquartile range = 8 to 24 weeks, maximum range = 7 days to 347 days).

Figure 2.1 - Age distribution of SIDS cases

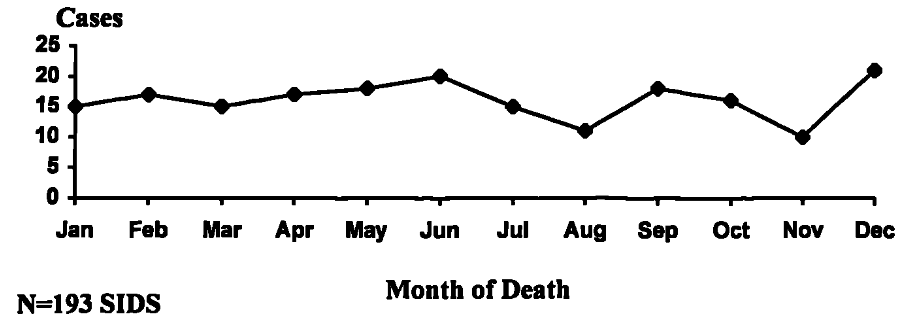


The smaller peak at 36 weeks appeared in the first year of the study, but was not evident in the second year.

Seasonal occurrence

Figure 2.2 shows the seasonal occurrence of the deaths over the 2 year period.

Figure 2.2 - Seasonal occurence



Deaths in Trent between 1st September 1993 and 31st January 1994 have been excluded to make the 3 regions comparable over the same time period. Clearly there was no winter peak and no overall pattern. Between 15 and 21 deaths occurred every month except for August and November when there were fewer. The lowest number of deaths occurred in November whilst the highest occurred the following month in December. A Kolmogorov-Smirnov test showed no significant deviation from the expected uniform distribution (p=0.2). Splitting these deaths into the first and second years of the study showed no underlying pattern.

Temporal occurrence

Table 2.3 shows the actual day of death. Although proportionately more deaths had

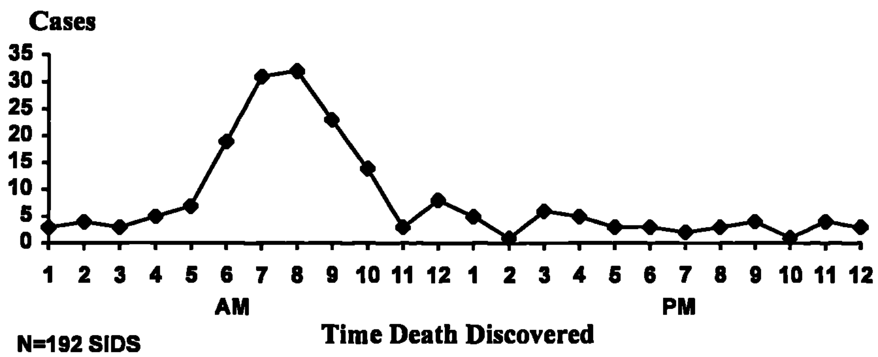
Table 2.3 - Day of death

Day of death	Number	%
Monday	29	13.4%
Tuesday	24	11.1%
Wednesday	24	11.1%
Thursday	38	17.6%
Friday	47	21.8%
Saturday	26	12.0%
Sunday	28	13.0%
N=216 SIDS		

occurred on Thursday & Friday, this was not significant when tested using the Kolmogorov-Smirnov Test (p=0.2).

Figure 2.3 shows the time of day the baby was found dead.

Figure 2.3 - Time death was discovered



N=192 SIDS

The figures given are only for those cases where an interview took place. Three further cases were excluded as they were taken to hospital and died later. Two thirds of the deaths (65.6%) were discovered between the hours of 5am and 10am. Between 1 to 8 deaths were found in each hour during the time interval 11am to 4am. A Kolmogorov-Smirnov test not surprisingly showed a significant deviation from the uniform distribution ($p<0.01$).

Location of parental home

Because of the way the controls were chosen the location of the parental home was partially matched to that of the index families. Figure 2.4 gives a rough indication of the type of location in which index families resided.

Table 2.4 - Location of parental home		
Location	Number	%
City (population > 150,000)	105	49.3%
Urban (population < 150,000)	70	32.9%
Village	34	16.0%
Rural	4	1.9%
N=213 SIDS		

Using mid-1995 population estimates in the South-West provided by the Office for National Statistics [175], the total population for Avon, Devon, Gloucestershire and Somerset was approximately 2.99 million (Cornwall was excluded in this calculation because of the absence of any major cities). The population of the major cities in those regions (Bristol, Exeter, Plymouth, Torbay, Gloucester, Cheltenham and Taunton) was 1.2 million (40.1%). This is a very crude estimate but gives us some idea of the population density. The breakdown of SIDS cases in Table 2.4 does not suggest an unexpected predominance in any one type of location.

Infant factors

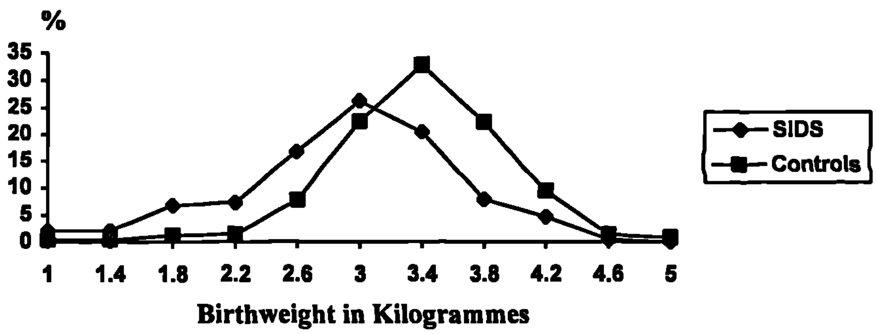
Sex

Of the SIDS cases, 60% were male compared to 50% of the controls. This difference was more than would be expected by chance (OR=1.52 [95% CI : 1.09 to 2.12]).

Birthweight

The birthweights ranged from 760g to 5390g. The median weight for the cases was 3005g (Interquartile range : 2578g to 3495g) compared to 3413g for the controls (Interquartile range : 3113g to 3719g).

Figure 2.4 - Birthweight



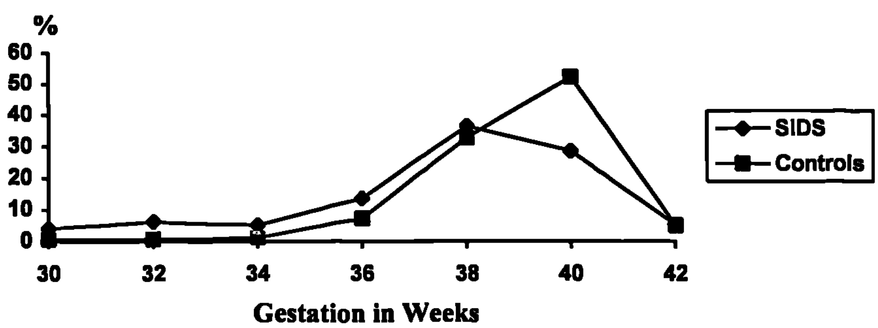
N=191 SIDS & 771 Controls

Significantly more of the SIDS infants (21.5% vs 4.3%) were born less than 2500g in weight compared to the control infants (OR=5.73 [95% CI : 3.33 to 9.85]). As a continuous variable, this difference in birthweight was significant ($p < 0.0001$).

However, weight at birth is dependent on the gestational age and sex of the baby. Therefore to investigate birthweight, gestational age and gender have to be taken into account using appropriate centile measurements.

Gestation

Figure 2.5 - Gestational age



N=191 SIDS & 767 Controls

The median gestation for the SIDS cases was 38 weeks and 2 days (Interquartile range : 36 weeks and 4 days to 39 weeks and 4 days) compared to 39 weeks and 2 days for the controls (Interquartile range : 38 weeks and 2 days to 39 weeks and 6 days). A difference of one week.

Significantly more SIDS infants (18.3% vs 4.4%) had a gestational age of less than 37 weeks compared to the controls (OR=4.53 [95% CI : 2.62 to 7.85]). As a continuous variable, this difference in gestational age was significant ($p<0.0001$).

Centile at birth

Centiles are calculated using the normal distribution of a baby's birthweight taking into account gestational age and gender. Similar to growth charts, a different distribution is used for boys and girls (the former are slightly heavier) and different distributions depending how long the infant was in the womb . The end result was a set of Z-scores (multiples of standard deviation from the normal mean for gestational age). If there was no real difference between the birthweights once gestational age and sex were taken into account, the shape of the Z-score distribution for both SIDS and controls would centre around zero deviations with an approximate bell-shaped curve.

Figure 2.6 - Centiles at birth (Z-Scores)

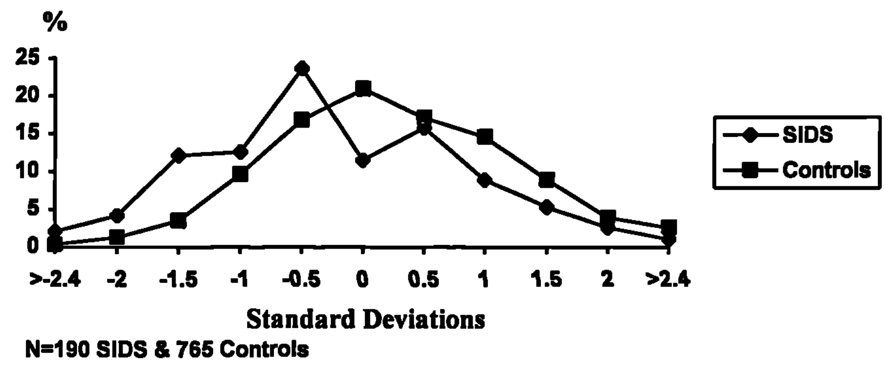


Figure 2.6 shows this characteristic distribution for the control infants but not for the SIDS infants. The Z-score distribution for the SIDS cases was shifted to the left, the median score was -0.36 standard deviations. Dichotomising the scores using zero as the cut-off, the difference between the two groups was significant (OR=2.28 [95% CI : 1.62 to 3.20]). As a continuous variable adjusted for matching, the birthweight centile was significant ($p<0.0001$). If the adjusted birthweight variable and the variables for

gestational age and sex were put in the same model, all three variables remained significant. The low birthweight of the SIDS infants cannot be explained by a shorter gestational age and remains lower despite the predominance of males.

Resuscitation at delivery

Just over a quarter of both index babies and controls (26.8% vs 25.4%) were resuscitated at delivery. Table 2.5 shows the resuscitation technique used and places them in descending order of use depending on the severity of the condition (the more severe the condition the further down the list one goes). For those infants where more than one technique was used, the technique that appeared lowest down the list was chosen.

Table 2.5 - Resuscitation technique

Technique	SIDS		Controls		OR [95% CI]
	N	%	N	%	
None	139	74.4	572	78.6	1.0 [Ref Group]
Oxygen only	18	9.6	89	12.2	0.83 [0.46 to 1.45]
Bag & mask	12	6.4	54	7.4	0.91 [0.43 to 1.79]
Intubation	12	6.4	10	1.4	p=0.0004*
CPR	6	3.2	3	0.4	p=0.003*

* Using Fisher's Exact Test
As a single parameter on 4 degrees of freedom p<0.001
N=187 SIDS & 728 Controls

The technique of suction for meconium was also asked for, although it was not felt that this could easily be placed into the above listing. These infants were excluded from this analysis if no other technique was used. Although the same proportion of index and control babies were resuscitated at delivery, more of the index babies required resuscitation using Intubation or CPR. This difference was significant (OR=6.04 [95% CI : 2.64 to 13.81]).

Admission to special care baby unit (SCBU)

Significantly more of the index infants (24.5% vs 7.4%) were admitted to a Special Care Baby Unit (SCBU) compared to the control infants (OR=3.97 [95% CI : 2.47 to 6.37]). The most common reasons were respiratory distress (SIDS=8.9%, controls=3.0%), prematurity (SIDS=4.7%, controls=1.2%), hypoglycaemia (SIDS=1.6%, controls=0.9%) and poor feeding (SIDS=2.1%, controls=0.5%).

Neonatal problems and congenital anomalies

More of the index infants (23.5%) were recorded as having neonatal problems compared to the control infants (10.1%). This difference was significant (OR=2.51 [95% CI : 1.61 to 3.91]). There was no single neonatal problem identified as being strongly characteristic of one group.

Slightly more of the index infants had congenital anomalies compared to the controls (10.9% vs 6.6%). This difference was not significant (OR=1.73 [95% CI : 0.98 to 3.04]). Most of the anomalies noted were not very serious although 5 of the SIDS infants had defects of the cardio-vascular system.

A full list of the neonatal problems and congenital anomalies are given in Appendix VII.

Maternal factors

Number of children

The number of children was defined as the number of livebirths born to the mother including the index or control infant, regardless of whether older children lived in the household, although most did. Index mothers had a median number of 2.86 children per family (range : 1 to 9 children) compared to 2.24 children for control mothers (range 1 to 6 children). Table 2.6 shows that proportionally more control mothers had one or two children, whilst proportionally more index mothers had three or more children.

Table 2.6 - Number of children

Number of children (including index or control infant)	SIDS N	SIDS %	Controls N	Controls %
1 child	50	25.6	323	41.4
2 children	55	28.2	275	35.3
3 children	54	27.7	124	15.9
4 children	23	11.8	38	4.9
5 children	4	2.1	14	1.8
6 children	5	2.6	6	0.8
7 or more children	4	2.1	0	0

N=195 SIDS & 780 Controls

Using the number of children as a dichotomous variable (cut-off being 3 or more children), index mothers had significantly more children than control mothers (OR=2.82 [95% CI : 1.74 to 4.51]). As a continuous variable, the number of children was significant ($p<0.0001$).

Multiple births

There were few multiple births, but of those there were, the majority occurred amongst the index mothers.

Table 2.7 - Multiple births				
Type of birth	SIDS		Controls	
	N	%	N	%
Singleton	185	94.9	775	99.4
Twin One	5	2.6	5	0.6
Twin Two	4	2.1	0	0
Triplet	1	0.5	0	0
N=195 SIDS & 780 Controls				

The numbers are very low but taking singletons as the reference group and utilising Fisher's Exact Test the resultant p-value was highly significant ($p=0.0001$).

Past obstetric history

Table 2.8 gives the past obstetric history in terms of previous miscarriages, stillbirths and terminations.

Table 2.8 - Obstetric history				
Previous history :	SIDS		Controls	
miscarriages	N=192	%	N=772	%
None	142	74.0	602	80.0
One	31	16.1	124	16.1
Two	12	6.3	31	4.0
Three	4	2.1	9	1.2
Four or more	3	1.6	6	0.8
stillbirths	N=192	%	N=772	%
None	190	99.0	764	99.0
One	2	1.0	8	1.0
terminations	N=192	%	N=769	%
None	164	85.4	676	87.6
One	22	11.5	80	10.4
Two	5	2.6	13	1.7
Three	1	0.5	0	0

The exact same proportion of index and control mothers have had one previous miscarriage, slightly more index mothers have had more than one. There was no significant difference whether no previous history was used as a reference group (OR=1.25 [95% CI : 0.85 to 1.82]) or one or less miscarriages as a reference group (OR=1.73 [95% CI : 0.93 to 3.11]). As a single parameter with 4 degrees of freedom the number of miscarriages was not significant ($p>0.05$). The same small proportion of index and control mothers (1.0%) had a previous stillbirth. A slightly greater proportion of index mothers have had one or more terminations, but the difference was not significant (OR=1.24 [95% CI : 0.76 to 1.99]). As a single parameter with two degrees of freedom (using 2 or more terminations as the final category) the number of terminations was not significant ($p>0.05$).

Duration from last pregnancy to this one

Over three quarters of the index mothers (76.3%) had a previous pregnancy (not necessarily a livebirth) compared to over two thirds of the control mothers (67.2%). The duration from the last pregnancy to the beginning of the recent pregnancy was much shorter for the index mothers. Twice as many index mothers (22.5% vs 10.7%) conceived within 6 months of the last pregnancy (OR=2.42 [95% CI : 1.44 to 4.03]).

Family factors

Marital status

The categories for marital status were initially taken from *The General Household Survey* [176]. The coding for being 'single' was described as 'not married and not living together'. However, it was clear from the response to this question that some mothers were not married or living with a partner but they did in fact have a partner and felt that they were in a supportive relationship. The category 'not married and not living together' was therefore split further into those with a partner and those who were single. Significantly more of the index mothers were unsupported by a partner at conception (OR=5.57 [95% CI : 2.89 to 10.83]), at birth (OR=4.15 [95% CI : 2.29 to 7.46] and at time of interview (OR=5.05 [95% CI : 2.73 to 9.35]). The proportion of unsupported mothers in both groups rose during this time period from conception to interview.

Table 2.9 - Marital status of mother						
	At conception		At birth		At interview	
Mothers supported by a partner	SIDS %	Controls %	SIDS %	Controls %	SIDS %	Controls %
Married	38.5	64.5	43.1	67.6	42.1	68.7
Living together	36.9	24.6	32.3	23.8	32.8	22.7
Partner but not living together	11.8	8.4	10.8	4.9	9.7	4.3
Total supported	87.2	97.5	86.2	96.3	84.6	95.7
Mothers unsupported						
Divorced/ widowed	0.5	0	0.5	0	0.5	0
Separated	1.0	0	1.5	0.8	3.6	1.2
Single	11.3	2.6	11.8	3.0	11.3	3.1
Total unsupported	12.8	2.6	13.8	3.8	15.4	4.3
N=195 SIDS & 778 Controls						

Support from relatives and friends

Because the mother did not have a partner it cannot be assumed that the mother felt unsupported. Obviously support can come from more than one direction. The mother was asked if there was support she could turn to if she was worried about the baby for any reason. Three sources were identified; grandparents, other family and friends.

Table 2.10 - Support from relatives and friends			
Source of support	SIDS	Controls	OR [95% CI]
Grandparents	75.6%	79.3%	0.81 [0.55 to 1.20]
*Other relatives**	60.6%	58.0%	1.11 [0.80 to 1.56]
Friends	67.9%	60.9%	1.36 [0.96 to 1.92]
N=193 SIDS & 778 Controls (* 779 Controls)			

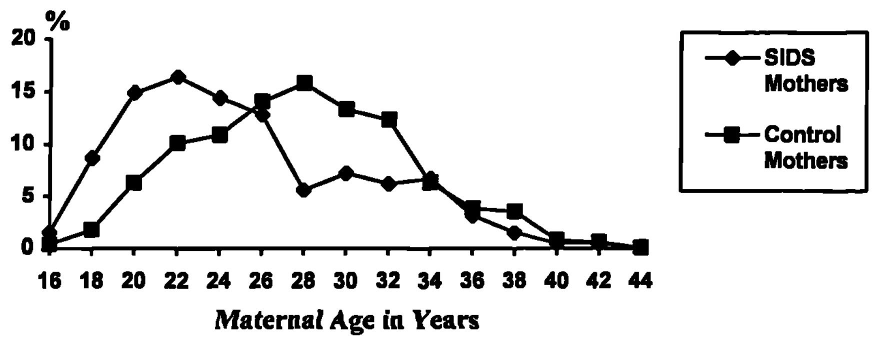
Although significantly more of the control mothers were supported by a partner, and had therefore the potential of a larger extended family, there was little difference in the amount of support both the index and control mothers felt they could turn to from relatives and friends. Fewer of the index mothers felt supported by grandparents, but a larger proportion of index mothers felt supported by other relatives. More of the index mothers felt supported by friends and neighbours, although this difference was not significant.

Parental age

(i) Maternal age

Figure 2.7 shows two very different age distributions for the index and control mothers. The median age of the index mothers was approximately 23 years and 3 months old compared to 26 years and 10 months old for the control mothers. As a continuous variable this difference was highly significant ($p < 0.0001$).

Figure 2.7 - Maternal age

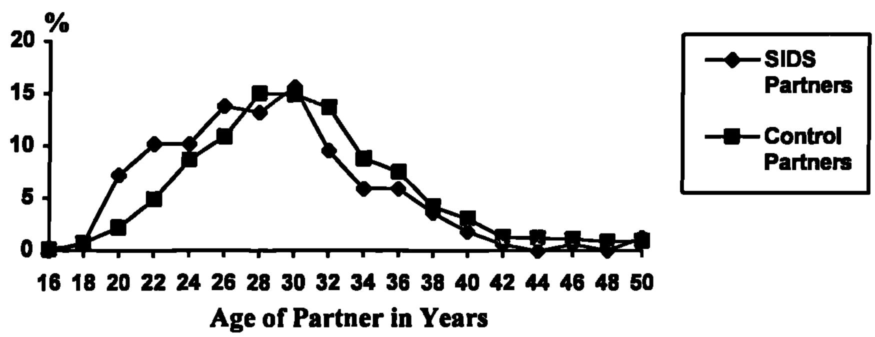


N=195 SIDS & 780 Controls

(ii) Age of partner

Figure 2.8 compares the age distributions of the index and control partners. As a continuous variable the difference between the two groups was significant ($p<0.0016$).

Figure 2.8 - Age of partner



N=167 SIDS & 759 Controls

The index partners (median age 27 years 6 months) were younger than the control partners (median age 28 years 11 months), although the age difference was not as marked as with the mothers.

(iii) Age difference of parents

Although it is clear that the index parents were younger, the above analysis does not give us any indication of the age difference between parents. Table 2.11 shows the median age difference if maternal age was subtracted from paternal age for different maternal age groups

Table 2.11 - Age difference of parents (partner - mother)

Maternal age	SIDS		Controls	
	N	Median Difference	N	Median Difference
≤18 years	15	+ 4.5 yrs	15	+ 3 yrs
19 - 20 years	22	+ 3.5 yrs	48	+ 4 yrs
21 - 25 years	59	+ 3.5 yrs	197	+ 2 yrs
26 - 30 years	40	+ 2 yrs	289	+ 2 yrs
31 - 35 years	26	0 yrs	257	+ 1 yr
≥36 years	5	+ 4 yrs	46	- 0.5 yrs

N=167 SIDS & 752 Controls

Taking the mother's age from the partner's age, the overall median age difference for the index parents was higher, the index partners were on average 2 years 6 months (interquartile range : +1 month to +5 years 3 months) older than the mothers, compared to the control partners, 1 year 5 months (interquartile range : -6 months to 4 years 4 months). However, as a continuous variable, parental age difference was not significant (p=0.32). For both index and control parents it appears that the age difference between mother and partner grew smaller as the age of the mother rose. The only anomaly being the group of index mothers over 35, but this group only contained 5 sets of parents in the index group.

<u>*Racial/ethnic group*</u>

(i) Mother's ethnic group

Table 2.12 shows the different ethnic groups for index and control mothers. The vast majority of both index and control mothers were white. There were slightly more non-whites amongst the cases but this difference was not significant (OR=1.28 [95% CI : 0.66 to 2.34]). There were significantly more Caribbean index mothers (p=0.043), but these numbers were very small and if all black origins were combined the difference compared to white mothers was not significant (OR=2.04 [95% CI : 0.62 to 5.95]). There were proportionally fewer Asian index mothers (2.6%) compared to controls

(4.5%) but this difference was not significant (OR=0.58 [95% CI : 0.18 to 1.52]). Using whites as the reference group and categorising the rest as black, Asians and mixed there was no significant difference when treating this variables as a single parameter on 3 degrees of freedom ($p<0.05$).

Table 2.12 - Mother's ethnic group				
Ethnic group	SIDS		Controls	
	N	%	N	%
White	179	91.8	729	93.5
Black (Caribbean)	6	3.1	8	1.0
Black (African)	0	0	2	0.3
Black (other)	0	0	2	0.3
Indian	1	0.5	10	1.3
Pakistani	4	2.1	21	2.7
Bangladeshi	0	0	3	0.4
Chinese/Japanese	0	0	1	0.1
Mixed race	5*	2.6	4**	0.5

* 2 Creole, 1 Anglo-Arab, 1 Anglo-Fijian, 1 Turkish-Spanish
** 1 Anglo-African, 1 Anglo-Jamaican, 1 Anglo-Arab, 1 mixed
N=195 SIDS & 780 Controls

(ii) Father's ethnic group

For ethnic group and country of birth, information was obtained from the father of the infant (not necessarily the current partner). The majority of fathers in both groups were white, although there were more non-whites amongst the index fathers, this difference was not significant (OR=1.56 [95% CI : 0.89 to 2.72]).

Table 2.13 - Father's ethnic group				
Ethnic group	SIDS		Controls	
	N	%	N	%
White	167	83.5	718	92.3
Black (Caribbean)	7	3.6	14	1.8
Black (African)	2	1.0	2	0.3
Black (other)	2	1.0	4	0.5
Indian	3	1.6	12	1.5
Pakistani	7	3.6	22	2.8
Bangladeshi	0	0	3	0.4
Chinese/Japanese	0	0	0	0
Mixed race	4*	2.1	3**	0.4

* 1 Anglo-Pakistani, 1 Anglo-Afro-Caribbean, 1 Egyptian-Arab, 1 Bengali-Arab
** 1 Anglo-Caribbean, 1 Anglo-African, 1 Anglo-Pakistani
N=192 SIDS & 779 Controls

There were proportionally more black index fathers, although this difference was just non-significant (OR=2.36 [95% CI : 1.00 to 5.29]). There were proportionally more Asian index fathers, this difference was also non-significant (OR=1.13 [95% CI : 0.49 to 2.37]).

(iii) Mother's country of birth

Slightly more of the index mothers were born outside the UK compared to the control mothers but this difference was not significant (OR=1.83 [0.90 to 3.53]).

Table 2.14 - Mother's country of birth				
Location of birth	SIDS		Controls	
	N	%	N	%
UK	180	92.3	746	95.6
Europe	8	4.1	11	1.4
Africa	1	0.5	4	0.5
Asia	5	2.6	16	2.1
Americas	0	0	2	0.3
Antipodes	1	0.5	1	0.1
N=195 SIDS & 780 Controls				

The numbers were too small to look at differences between each country. Grouping by continents and comparing mothers born in different continents showed no significant differences except for a higher proportion of non-UK European SIDS mothers (p=0.022), although the numbers were very small.

(iv) Father's country of birth

Slightly more of the index fathers were born outside the UK but this difference was not significant (OR=1.66 [95% CI : 0.87 to 3.06]).

Table 2.15 - Father's country of birth				
Location of birth	SIDS		Controls	
	N	%	N	%
UK	175	91.1	735	94.4
Europe	5	2.6	5	0.6
Africa	1	0.5	6	0.8
Asia	10	5.2	26	3.3
Americas	0	0	5	0.6
Antipodes	1	0.5	2	0.3
N=192 SIDS & 779 Controls				

Comparing those fathers born in the UK with those born in a different continent, showed no significant differences.

Socio-economic factors

There were several socio-economic markers built into the questionnaire, based on occupation, education and family income.

Marker 1 : occupational classification (social class)

This classification is taken from the *Standard Occupational Classification* [177]. The underlying basis of this system is to classify people in terms of expected mortality given their occupation. The expected life-expectancy is higher for people in managerial or professional occupations and lower for those in unskilled labour. People in the armed forces, students and those unemployed are not classified.

The categories are as follows :

I Professional occupations
II Managerial and technical occupations
III Skilled occupations : (N) non-manual (M) manual
IV Partly skilled occupations
V Unskilled occupations

Until recently the classification was based on the occupation of the 'head of the household', usually the male. Given the shifting trend of higher female employment status in the household it was no longer appropriate to assume the male has the 'better' occupation. Classification is now usually based on both the mother and partner (if applicable), the head of the household chosen as the one with the longest life-expectancy given their occupation.

Table 2.16 shows that more control families fell into the classes I, II, III non-manual, and a similar proportion of index and control families were found in classes IV and V. The startling observation however from the first two columns of the table, show that for nearly a half of the index families, both parents were unemployed compared to less than a sixth of the control parents.

Table 2.16 - Occupational classification				
Classification	Using current occupation		Using current or previous occupation	
	SIDS%	Controls %	SIDS %	Controls %
I	2.1	5.3	2.1	5.4
II	10.3	24.2	13.3	28.6
III (non-manual)	6.7	11.3	11.3	14.5
III (manual)	21.5	30.0	33.3	33.5
IV	10.3	9.2	19.5	10.5
V	2.1	2.1	5.6	1.7
Unemployed	44.6	15.4	13.3	4.1
Student	2.6	1.2	1.5	0.6
Armed Forces	0	1.1	0	1.2

Shaded areas represent groups not included in the classification
N 195 SIDS & 780 Controls

Clearly the unemployed status of many families effects this measure of socio-economic status. The unemployed cannot be classified because they are not an homogeneous group, an unemployed professional is different from an unemployed unskilled worker. This problem is overcome if unemployed families are classified using previous employment. Even in doing this Table 2.16 shows that 26 sets of index parents (13.3%) and 32 sets of control parents (4.1%) were not only unemployed but also had never been employed. However the unemployed group could now be considered more homogeneous and could be placed in the lower socio-economic group of the classification system.

Again more control families were classified in the higher social groupings, the same proportion were classified as III (manual) and more index families were classified in the lower social groupings. Dichotomising the classification into I, II, III (non-manual) compared to III (manual), IV, V and the unemployed, the difference was significant (OR=2.63 [95% CI :1.79 to 3.89]).

Marker 2 : family income

One of the reasons why occupational classification is so often used as a measure of socio-economic status in UK studies (compared for instance to those conducted in the US) is because of the reluctance of individuals to disclose the amount of money they earn. However the response rates to questions of family income in this study were very high (97.4% for the SIDS parents and 98.7% for control parents). This was probably due to several factors. The interviewers were all trained health professionals, experienced at building up trusting relationships with the parents, and the confidential nature of the study was continually emphasised. Another reason may also have been the non-specific way in which the question was asked, rather than ask directly for the amount of weekly income, the income was split up into six specific bands from which the parents could choose. Table 2.17 compares the weekly family income between the SIDS and control families.

Table 2.17 - Weekly family income

Family income	SIDS %	Controls %
£0 - £59	12.6	2.7
£60 - £99	30.5	17.9
£100 - £199	32.6	27.8
£200 - £299	14.7	27.7
£300 - £499	6.8	17.3
£500+	2.6	6.6
N 190 SIDS & 770 Controls		

Nearly five times as many SIDS families had an average weekly income of less than £60 a week compared to control families. Comparing those families who received less than £200 a week, the difference was significant (OR=3.34 [95% CI : 2.29 to 4.86]). This discrepancy may partly be explained by the excess of single mothers in the SIDS group. Table 2.9 previously showed that 15.4% of SIDS mothers were single at the time of interview compared to only 4.3% of control mothers. Excluding single mothers, the risk associated with weekly family income slightly reduced but remained highly significant (OR=3.04 [95% CI : 2.05 to 4.50]).

The questionnaire also asked if the families were receiving Income Support (IS), now known as Family Credit, at the time of interview. Two thirds of the index families (66.0%) responded that they received IS, compared to 28.2% of control families (OR=6.27 [95% CI : 4.15 to 9.47]). Excluding single mothers there was still a highly significant difference between the two groups (OR=4.85 [95% CI : 3.35 to 7.05]).

Marker 3 : parental education

Another way of measuring socio-economic status was to use parental education. Table 2.18 shows the highest qualification attained by both mothers and partners as well as giving an overall grading to each family using the highest qualification attained by either parent.

Table 2.18 - Parental education						
Qualification	Mother		Partner		Parents*	
or equivalent	N=193	N=775	N=166	N=699	N=193	N=776
	SIDS %	Controls %	SIDS %	Controls %	SIDS %	Controls %
Degree	2.6	7.1	4.8	10.7	4.7	12.2
Higher education	2.6	8.9	4.2	9.6	5.2	11.6
'A' level	7.3	9.0	7.2	10.6	9.8	13.9
'O' level	29.5	33.5	26.5	27.8	36.3	34.7
Below 'O' level	17.1	22.5	23.5	22.6	19.7	16.5
None	40.9	19.0	33.7	18.7	24.4	11.0
* Highest qualification of mother or partner						

Both index mothers and partners showed a markedly lower degree of academic achievement compared to the control parents. In the index families, twice as many parents had no educational qualifications compared to control families. Looking at the highest qualification attained by either parent, significantly fewer of the index parents achieved 'A' level status or higher (OR=2.46 [95% CI : 1.62 to 3.72]).

Housing

Along with establishing markers for socio-economic status, several questions were asked regarding family accommodation, type of house, tenure, the council tax band, condition of the house, number of rooms and the number of people in the household.

(i) Type of housing

Table 2.19 shows the type of housing the SIDS and control families lived in. The condition of housing types was too varied to make any strong assumptions about which type constituted 'good' or 'bad' accommodation.

Table 2.19 - Type of housing				
	SIDS		Controls	
	N	%	N	%
Detached	10	5.1	91	11.7
Town house	0	0	8	1.0
Bungalow	0	0	2	0.3
Semi-detached	72	36.9	308	39.5
Terraced	71	36.4	305	39.2
Maisonette	2	1.0	11	1.4
Purpose-built flat	20	10.3	38	4.9
Converted flat/room	10	5.1	11	1.4
With business	3	1.5	11	1.4
Mobile home	5	2.6	0	0
B&B /hostel	2	1.0	0	0
N=195 SIDS & 779 Controls				

However, taking the two extremes, twice as many control families lived in what may be regarded as the more expensive type of accommodation (detached homes), whilst 7 of the index families lived in what may be regarded as less desirable accommodation (caravans, hostels, bed and breakfast accommodation) compared to none of the controls.

(ii) Tenure of housing

Table 2.20 shows the tenure of housing. Twice as many control families had a more secure tenure (ie mortgage or house-owner) compared to the index families. This difference was significant (OR=4.19 [95% CI : 2.86 to 6.13]).

Table 2.20 - Tenure of housing				
Tenure	SIDS		Controls	
	N	%	N	%
Owned house	4	2.1	32	4.1
Paying mortgage	53	27.2	454	58.3
Rent-council	78	40.0	180	23.1
Rent-housing association	15	7.7	30	3.9
Rent-private (furnished)	13	6.7	21	2.7
Rent-private (unfurnished)	17	8.7	44	5.6
With job/business	3	1.5	6	0.8
Living with relatives	6	3.1	11	1.4
Owned caravan	4	2.1	0	0
Owned by trust	2	1.0	1	0.1
N=195 SIDS & 779 Controls				

(iii) Council tax band

Unfortunately, at the time of this study the classification of housing into Council Tax Bands was a relatively new house-rating system and many of the index (39.6%) and control parents (27.6%) were not aware of their own particular council tax band.

Table 2.21 - Council Tax Band				
Band	SIDS		Controls	
	N	%	N	%
A	83	71.6	282	50.1
B	14	12.1	135	24.0
C	14	12.1	72	12.8
D	3	2.6	46	8.2
E	1	0.9	17	3.0
F	1	0.9	8	1.4
G	0	0	3	0.5
H	0	0	0	0
N=116 SIDS & 563 Controls				

Table 2.21 shows that significantly more of the control families (13.1%) lived in the higher-rated accommodation (D,E,F and G) compared to the index families (4.4%). This difference was significant (OR=3.36 [95% CI : 1.33 to 10.89]).

(iv) Condition of house

Families were asked about various problems with the house and how serious this problem was. Table 2.22 shows the proportion of families where the problem was fairly or very serious.

Table 2.22 - Problems with house					
	SIDS		Controls		OR [95% CI]
Specific problems	N	%	N	%	
Damp or condensation	33	17.1	73	9.4	1.99 [1.23 to 3.16]
Mould	26	13.5	36	4.6	3.21 [1.80 to 5.63]
Leaky roof	4	2.1	5	0.6	p=0.51**
*Leaks from elsewhere**	20	10.4	27	3.4	3.47 [1.78 to 6.67]
Any of these problems affect the baby's room	26	13.5	56	7.2	1.82 [1.06 to 3.14]
* eg badly fitting windows and doors ** Fisher's exact test N=193 SIDS & 778 Controls					

Significantly more of the index families lived in housing with problems of damp, condensation, mould and leaks from badly fitting doors and windows. At least one of these problems affected nearly twice as many SIDS infants compared to the controls. The major problems listed were condensation on the windows, cold and draught and damp walls with resultant mould.

(v) Number of people and rooms in the household

The median number of rooms, excluding the bathroom, toilet if separate, hallways and kitchen (if not used as a dining room) in the index household was 4 (range 1 to 10), whilst the median number in the control household was 5 (range 2 to 12). Proportionally more of the SIDS families (26.8% vs 15.8%) had 3 rooms or fewer compared to the controls (OR=1.92 [95% CI : 1.29 to 2.82]).

The median number of people (including young adults, children and infants) living in all households was 4 (range 2 to 20). Because a greater proportion of index mothers were single, a larger proportion of index households had just two people in the household (index mother and baby), but this difference was not significant ($p=0.06$). Conversely, and partly because the index mothers had a greater number of children, a larger proportion of index families had more people living in the household. Twice as many index families had 6 or more people living in their households (21.5% vs 9.9%) compared to control families (OR=2.51 [95% CI : 1.61 to 3.86]).

Dividing the number of people in the household by the number of rooms (thus if 3 people shared 6 rooms, the score would be 0.5) a measure of overcrowding can be derived. The results are given in Table 2.23. Clearly these calculations show that index families had much less space per household compared to the controls.

Table 2.23 - Number of persons per room				
People per room	SIDS		Controls	
	N	%	N	%
0.25	0	0	16	2.1
0.5	3	1.5	31	4.0
0.75	58	29.9	364	46.8
1	57	29.4	204	26.2
1.25	38	19.6	119	15.3
1.5	8	4.1	16	2.1
1.75	9	4.6	22	2.8
2.0	10	5.2	5	0.6
> *2.0*	11	5.7	1	0.1
N–194 SIDS & 778 Controls				

As a continuous variable, the difference was highly significant ($p<0.0001$). Twice as many index families lived in accommodation where there was less than 1 room available for each member of the household compared to the controls (39.2% vs 20.9%). This difference was significant (OR=2.56 [95% CI : 1.76 to 3.72]). At the extremes, 10.9% of index families lived two or more people to a room (in one family, five people to a room), compared to only 0.7 % of control families.

Chapter 11

Univariable Analysis of Primary Hypotheses

1 Sleeping position

The positions in which the SIDS infants and the controls were put down to sleep, found after sleep for the last/reference sleep and usually put down are shown in Table 2.24.

Table 2.24 - Sleeping position					
Position :	SIDS		Controls		OR [95% CI]
Put Down	N=188	%	N=774	%	
Back	82	43.6	509	65.8	1.00 [Ref Group]
Side	76	40.4	241	31.1	2.01 [1.38 to 2.93]
Front	30	16.0	24	3.1	9.58 [4.86 to 18.87]
Found	N=187	%	N=755	%	
Back	67	35.8	618	81.9	1.00 [Ref Group]
Side	43	23.0	92	12.2	4.51 [2.65 to 7.66]
Front	77	41.2	45	6.0	21.36 [11.67 to 39.08]
Usually	N=195	%	N=780	%	
Back	93	47.7	497	63.7	1.00 [Ref Group]
Side	78	40.0	258	33.1	1.63 [1.13 to 2.35]
Front	24	12.3	25	3.2	6.29 [3.19 to 12.40]
For all 3 variables as a single parameter on 2 degrees of freedom $p<0.001$					

The prone position was the least common sleeping position in which infants were put down, but carried the greatest risk. Side-sleeping position carried a significantly increased risk when compared with supine. The odds ratios for position found rather than put down were in the same direction but much stronger. A change in position during the reference sleep from side to prone was rare amongst the controls (9 of 238=3.8%) compared to the SIDS victims (29 of 74=39.2%), whilst conversely the change from side to supine was rare amongst the SIDS victims but common amongst the controls. The major risk factor was for infants put down on their side and found prone (OR=21.69 [95% CI : 8.84 to 53.20]), rather than for infants who remain on their side or roll to supine (OR=1.21 [95% CI : 0.79 to 1.87]). The risk estimates associated with the usual practice of how the infants were put down was not as great but still significant for both side and prone.

Evidence from this study showed that the side-sleeping position was unstable. Current advice to parents regarding SIDS includes extending the lower arm of the infant if laid down on the side to prevent rolling to the prone position. However if we divide the infants put down into their side into those who had their lower arm extended (OR=1.84 [95% CI : 1.18 to 2.85] and those who did not (OR=2.13 [95% CI : 1.31 to 3.40]), the risk remained significant regardless of whether the lower arm was extended or not.

2 Thermal environment

Maternal anxiety over infant's thermal environment

Some mothers worry about their baby getting too cold, others worry about the baby getting too hot. The mothers were asked which they worried about most.

Table 2.25 - Maternal anxiety over infant's thermal environment

Mother worried about :	SIDS		Controls		OR [95% CI]
	N	%	N	%	
Neither	40	20.7	126	16.2	1.00 [Ref Group]
Too hot	53	27.5	359	46.1	0.47 [0.28 to 0.79]
Too hot or cold	45	23.3	163	20.9	0.89 [0.52 to 1.51]
Too cold	55	28.5	131	16.8	1.29 [0.76 to 2.19]

As a single parameter on 3 degrees of freedom p<0.001
N=193 SIDS & 779 Controls

Significantly more of the control mothers worried about their baby getting too hot compared to the index mothers, suggesting a protective effect. Roughly the same proportion of index and control mothers worried about their baby becoming too hot or cold, whilst more of the index mothers worried about their baby becoming cold, although this difference was not significant. Alternatively we could adopt a reference group that contains both those mothers who were not anxious and those mothers who were anxious about their infant being both too hot or too cold. Again, significantly more of the control mothers worried about their baby being too hot (OR=0.50 [95% CI : 0.34 to 0.74]), whilst more index mothers worry about their baby being too cold (OR=1.43 [95% CI : 0.94 to 2.16]), which just failed to reach significance.

Tog values

The thermal resistance (tog value) of bedding and clothing for sleep, usually, and during the last/reference sleep for SIDS victims and controls is shown in Table 2.26. The SIDS infants were more heavily wrapped than the controls, both usually for day and night sleeps and during the last/reference sleep, the risk increasing with greater tog values. The difference in median tog values between index and control infants was approximately 1 tog for each time period measured.

Table 2.26 - Tog values

Tog Values :	SIDS		Controls		OR [95% CI]	OR [95%CI]*
Usually by night	N=193	%	N=779	%		
< 6 togs	81	42.0	391	50.2	1.00 [Ref Group]†	1.00 [Ref Group]†
6-9 togs	80	41.5	318	40.8	1.27 [0.86, 1.87]	1.27 [0.83, 1.95]
≥ 10 togs	32	16.6	70	9.0	2.27 [1.32, 3.90]	1.65 [0.90, 3.04]
Usually by day	N=193	%	N 778	%		
< 6 togs	135	70.0	643	82.6	1.00 [Ref Group]†	1.00 [Ref Group]‡
6-9 togs	43	22.3	117	15.0	2.00 [1.26, 3.15]	2.07 [1.24, 3.46]
≥ 10 togs	15	7.8	18	2.3	4.32 [1.97, 9.46]	3.94 [1.64, 9.49]
When put down	N=191	%	N=779	%		
< 6 togs	90	47.1	456	58.5	1.00 [Ref Group]†	1.00 [Ref Group]†
6-9 togs	68	35.6	263	33.8	1.50 [0.99, 2.26]	1.52 [0.96, 2.42]
≥ 10 togs	33	17.3	60	7.7	3.38 [1.94, 5.87]	2.78 [1.49, 4.16]
When found	N=190	%	N=779	%		
< 6 togs	112	58.9	556	71.4	*1.00 [Ref Group]†*	*1.00 [Ref Group]†*
6-9 togs	51	26.8	183	23.5	1.61 [1.05, 2.47]	1.57 [0.97, 2.54]
≥ 10 togs	27	14.2	40	5.2	4.41 [2.20, 7.62]	3.52 [1.74, 7.11]

† As a single parameter on 2 degrees of freedom p<0.001
‡ As a single parameter on 2 degrees of freedom p<0.025
* Controlled for socio-economic status (using Income Support)

Previous studies [26], have shown that heavy wrapping was associated with low socio-economic status. If we control for this using Income Support as a proxy measure (the final column of Table 2.26), heavy wrapping still remained a significant factor.

Wearing a hat

The question was asked as to whether the baby wore a hat when sleeping by night or day or during the last sleep.

Table 2.27 - Whether infant wore a hat during sleep

Infant wore a hat :	SIDS		Controls		OR [95% CI] or p-value
	N	%	N	%	
Usually for night sleeps	6	3.1	1	0.1	p=0.0003*
Usually for day sleeps†	28	14.4	14	14.6	OR=0.98 [0.61 to 1.56]
Put down for last sleep††	10	5.2	14	1.8	p=0.02*
Found after last sleep	9	4.7	12	1.5	p=0.02*

* Using Fisher's Exact Test
N=193 SIDS & 779 Controls † =194 SIDS †† =192 SIDS

Very few babies seemed to have worn a hat for the usual night sleep, but significantly more of the index babies adhered to this practice than control babies. Wearing a hat for the day sleep was much more common, approximately the same proportion of control and index babies wore a hat. Regarding the last sleep, which could have been a night or day sleep, significantly more of the index babies wore a hat. Only 1 of the index babies and 2 of the controls were without their hat when found after the last sleep.

The numbers here were too small to come to any firm conclusions but it appears that more of the index babies were in the practice of wearing hats for night-time sleep and wore a hat for the last sleep.

Use of an electric blanket

Very few of the babies were given an electric blanket either usually or at the time of the last sleep. Only one index infant always used an electric blanket at night (this was for the whole sleep), compared to two of the controls (one mother switched on the blanket for two hours, the other mother only to warm the bed before the infant was put down to sleep). During the day, only one control infant used an electric blanket (for just one hour). At the time of last sleep one index infant used an electric blanket for the whole period and one control infant for two hours, this was their usual practice.

Use of a hot water bottle

Few of the babies used a hot water bottle for their usual night sleep. Only 7 of the cases (3.6%) ever used a hot water bottle compared to 16 of the control babies (2.1%), this difference was not significant (Fisher's Exact Test : $p=0.20$). For only 1 case and 1 control was the hot water bottle actually in the bed with baby. Even fewer babies had a hot water bottle for their usual day sleeps. Only 2 of the cases (1.0%) had a hot water bottle compared to just 1 control (0.1%). This difference was not significant (Fisher's Exact Test : $p=0.10$). For only 1 of these cases was a hot water bottle in bed with the baby. Very few babies had a hot water bottle for the last sleep, 2 SIDS infants (1.0%) and 4 control infants (0.5%). The difference between the cases and controls was not significant (Fisher's Exact Test : $p=0.35$). For 3 of the controls and 1 of the cases the bottle was taken out of the bed when the baby was put in it. For the other control the bottle was in the bed for only 2 minutes with the baby and for the other case the bottle was in the bed until it went cold.

Heating in room for last/ reference sleep

Heating was a difficult question to answer because of the number of different heating systems, types of setting and how the setting was arranged for different rooms. This was further complicated by systems such as storage heaters (which may be 'on' during the night but not necessarily giving out heat) and systems that tried to maintain a constant temperature so therefore came on intermittently rather than at a pre-set time. Furthermore, many of the responses to 'usual practice' were dependent on outside temperature and the number of people in the house.

One of the essential questions to answer was whether the heating was on for the duration of the last sleep. Thus, from several pieces of data (including the time and setting of heating, type of heating, room the baby slept in and narrative account) this information was gathered. The period of the last sleep was calculated from the time the baby was last seen or heard to the time the baby was found after the sleep. For houses where the main type of heating was a night storage system, it was not assumed the heating was on, unless specifically stated. Responses were calculated for 188 SIDS infants and 772 controls.

Twice as many of the index babies (21.8%) slept in a room where the heating was on for the whole duration compared to the controls (11.9%). This difference was significant (OR=2.14 [95% CI : 1.30 to 3.50]). Of the index sleeps, 9 were during the day compared to 35 of the controls, this at a time when the heating was more likely to be on during the whole of the sleep. If we compare heating for the whole duration of the night sleep only, the significance increased (OR=2.57 [95% CI : 1.56 to 4.19]).

How often was the window open or door ajar

The mothers were asked how often the window was open or the door ajar in the room in which the baby slept. There was no difference between the two groups during usual night or day sleeps. On the night of the last/reference sleep, slightly more control households had both the window open (21.9% vs 24.6%) and the door ajar (64.5% vs 68.5%) but these differences were not significant (OR=0.86 [95% CI : 0.57 to 1.28] and OR=0.84 [95% CI : 0.59 to 1.19], respectively).

Arrangement of bedding

The type of bedding, how the bedding was arranged and where the infant was put in the bed is shown in Table 2.28.

Table 2.28 - Arrangement of bedding for last /reference sleep					
Type of arrangement :	SIDS		Controls		OR [95% CI]
Duvet used	N=194	%	N=779	%	
No	112	57.7	602	77.3	1.00 [Ref Group]
Yes	82	42.3	177	22.7	2.82 [1.95, 4.08]
Bedding tucked	N=185	%	N=774	%	
Tucked in or no bedding	82	44.3	467	60.3	1.00 [Ref Group]
Lying loosely over	103	55.7	307	39.7	1.92 [1.35, 2.73]
Placement of infant	N=172	%	N=702	%	
Top or middle of bed	169	98.3	689	98.1	1.00 [Ref Group]
Bottom of bed	3	1.7	13	1.9	p=1.0*
* Using Fisher's Exact Test					

Significantly more of the SIDS infants slept under a duvet for the last/reference sleep. This result remained significant for both the usual day (OR=2.64 [95% CI : 1.57 to 4.44]) and night sleeps (OR=1.83 [95% CI : 1.27 to 2.64]). Of those infants that slept under a duvet for the last/reference sleep, 23.5% of SIDS infants slept under the parental duvet compared to 13.0% of control infants. The use of duvet covering remained significant when adjusted for bed-sharing (OR=2.38 [95% CI : 1.61 to 3.50]).

Significantly more of the SIDS infants also slept with loose covering for the last/reference sleep. This was also the finding for the usual night sleep (OR=2.72 [95% CI : 1.11 to 6.65]) but not the usual day sleep (OR=0.87 [95% CI : 0.61 to 1.23]). The risk associated with loose covering for the last/reference sleep, remained significant when adjusted for either bed-sharing or duvet use, but became non-significant when adjusted for both (OR=1.41 [95% CI : 0.96 to 2.06]).

Very few SIDS or control infants were put down to sleep at the bottom of the bed; either for usual sleep or for the last/reference sleep. Significantly more SIDS infants (9.0% Vs 3.2%) were found at the bottom of the bed after the last/reference sleep (OR=3.02 [95% CI : 1.42 to 6.25]).

Found with covers over the head

We asked the parents whether the baby had been found with bed covers over the head either usually or for the last/reference sleep.

Table 2.29 - Found with covers over the head					
Covers over head:	SIDS		Controls		OR [95% CI]
Usually	N=192	%	N=779	%	
Never/Sometimes	181	94.3	763	98.0	1.00 [Ref Group]
Often/ Always	11	5.7	16	2.1	2.72 [1.11 to 6.65]
After last sleep	N=182	%	N=765	%	
No	148	81.3	747	97.7	1.00 [Ref Group]
Yes	34	18.7	18	2.3	18.93 [8.05 to 44.48]

Table 2.29 shows that a small but significant proportion of SIDS infants have been found previously either often or always with covers over their head after a sleep. A much greater group of SIDS infants were found with covers over their head after the last sleep compared to control infants.

3 Smoking

Maternal smoking

The mother was asked what type of cigarettes she smoked at the time of interview. Many more index mothers smoked (71.3%) compared to control mothers (29.7%). This difference was significant (OR=5.86 [95% CI : 4.10 to 8.44]).

Table 2.30 - Type of cigarette mother smokes				
Type of cigarette	SIDS		Controls	
	N	%	N	%
None	56	28.7	548	70.3
Filter (low tar)	91	46.7	137	17.6
Filter	34	17.4	85	10.9
Non-filter	2	1.0	0	0
Hand-rolled	10	5.1	10	1.3
Any	2	1.0	0	0
N=195 SIDS & 780 Controls				

Most of the mothers smoked filtered cigarettes (90% of the index mothers and 95.7% of the controls) although slightly more index mothers smoked low tar cigarettes (65.5% of index mothers who smoked compared to 59.1% of control mothers).

The mother was also asked about her smoking habits before, during and after pregnancy.

Table 2.31 - Maternal smoking, before, during and after pregnancy						
Before pregnancy	During pregnancy	After pregnancy	SIDS		Controls	
			N	%	N	%
Non-smoker	*Non-smoker*	*Non-smoker*	52	26.7	515	66.0
Smoker	*Non-smoker*	*Non-smoker*	7	3.6	32	4.1
Non-smoker	*Smoker*	*Non-smoker*	0	0	0	0
Non-smoker	*Non-smoker*	*Smoker*	5	2.6	6	0.8
Smoker	*Smoker*	*Non-smoker*	7	3.6	24	3.1
Smoker	*Non-smoker*	*Smoker*	9	4.6	31	4.0
Non-smoker	*Smoker*	*Smoker*	0	0	4	0.5
Smoker	*Smoker*	*Smoker*	115	59.0	168	21.5
N=195 SIDS & 780 Controls						

There appeared to be a minimal change in habit throughout these three time periods. The majority of mothers in both groups (85.7% index mothers and 87.5% control mothers) either remained non-smokers or maintained their smoking habit before, during and after pregnancy. Not surprisingly the odds ratios for these 3 periods are very similar (before pregnancy : OR=5.07 [95% CI : 3.45 to 7.45], during pregnancy : OR=4.84 [95% CI : 3.33 to 7.04], after pregnancy : OR=5.19 [95% CI : 3.57 to 7.55]).

The high correlation between the time periods suggests we cannot treat these 3 variables as separate independent factors. The analysis will mainly concentrate on smoking during pregnancy as the proxy measure for maternal smoking but will use maternal smoking after pregnancy where appropriate.

Table 2.32 shows the risk associated with the number of cigarettes smoked during pregnancy.

Table 2.32 - Maternal smoking during pregnancy : dose-response effect					
Cigarettes smoked a day	SIDS		Controls		OR [95% CI]
	N	%	N	%	
Non-smoker	73	37.4	584	74.9	1.00 [Ref Group]
1-9 cigarettes	53	27.2	108	13.8	4.59 [2.71 to 7.77]
10-19 cigarettes	42	21.5	58	7.4	5.38 [2.96 to 9.75]
20+ cigarettes	27	13.8	30	3.8	7.88 [3.87 to 12.26]
As a single parameter on 3 degrees of freedom p<0.001					

Clearly there was a strong dose-response effect, the more the mother smoked during pregnancy the greater the associated risk.

Paternal smoking

Many more of the index partners smoked (60.5%) compared to the control partners (36.2%). This difference was significant (OR=3.04 [95% CI : 2.13 to 4.13]). The non-smoking reference group in this calculation included mothers who did not have a partner. If we exclude single mothers from both groups the odds ratio slightly increased (OR=3.30 [95% CI : 2.25 to 4.82]). Table 2.33 shows the dose-response effect for paternal smoking. The odds ratio was significant for each number of cigarettes smoked, although the gradient was not linear.

Table 2.33 - Smoking habits of partner : dose-response effect

Cigarettes smoked a day	SIDS N	SIDS %	Controls N	Controls %	OR [95% CI]
Non-smoker	77	39.5	498	63.8	1.00 [Ref Group]
1-9 cigarettes	33	16.9	100	12.8	2.18 [1.28 to 3.69]
10-19 cigarettes	52	26.7	112	14.4	3.81 [2.31 to 6.29]
20+ cigarettes	33	16.9	70	9.0	3.50 [1.86 to 6.56]

Other people smoking in the household

Table 2.34 shows the number of other people who smoke in households (excluding mothers and their partners).

Table 2.34 - Other people smoking in the household

	SIDS N	SIDS %	Controls N	Controls %
No other people	167	85.6	734	94.1
At least one grandparent	17	8.7	35	4.5
At least one sibling	2	1.0	2	0.3
At least one other relative	8	4.1	14	1.8
At least one non-relative	8	4.1	6	0.8

In each group, proportionally more of the index households had other smokers compared to the control households. In some households people from more than one group were smokers, hence the disparity in the percentages given. If we just look at whether a household had **at least** one other smoker (ie counting households with smokers from several groups just once) then the results show that 14.3% of index households had at least one smoker other than the parents compared to 5.9% of the control households. This difference was significant (OR = 2.99 [95% CI : 1.71 to 5.25]).

Table 2.35 - Other people smoking in the household : dose-response effect					
Cigarettes smoked a day	SIDS		Controls		OR [95% CI]
	N	%	N	%	
Non-smoker	167	85.6	734	94.1	1.00 [Ref Group]
1-9 cigarettes	6	3.1	15	1.9	p=0.257†
10-19 cigarettes	7	3.6	15	1.9	p=0.161†
20+ cigarettes	15	7.7	16	2.1	4.12 [1.85 to 9.08]
† Using Fisher's Exact Test, combining these 2 groups : OR–1.96 [0.93 to 4.13]					

Table 2.35 shows the dose-response effect of other people who smoked in the household. Although the numbers are small, the risk to the infant increased when others in the household smoked 20 or more cigarettes a day.

<u>*Postnatal exposure*</u>

(i) Number of smokers in the household

Using maternal smoking after pregnancy we can look at the total number of smokers in each household.

Table 2.36 - Number of smokers in the household						
Mother after pregnancy	Partner smoking	Others in the household	SIDS		Controls	
			N	%	N	%
Non-smoker	*Non-smoker*	*Nobody*	29	14.9	407	52.2
Smoker	*Non-smoker*	*Nobody*	32	16.4	60	7.7
Non-smoker	*Smoker*	*Nobody*	36	18.5	154	19.7
Non-smoker	*Non-smoker*	*Somebody*	4	2.1	14	1.8
Smoker	*Smoker*	*Nobody*	70	35.9	113	14.5
Smoker	*Non-smoker*	*Somebody*	12	6.2	17	2.2
Non-smoker	*Smoker*	*Somebody*	4	2.1	9	1.2
Smoker	*Smoker*	*Somebody*	8	4.1	6	0.8
N–195 SIDS & 780 Controls						

At the time of interview, at least one person smoked in 85.1% of the index households compared to 47.8% of the control households. At least two people smoked in over half of the index households (48.2%) compared to 18.6% of control households.

We asked the parents three questions about which rooms smoking were allowed to take place in. For each of these questions only 1 index and 2 control families did not respond. Firstly we asked if smoking was allowed in the room where the baby slept when the baby was not present. This was far more common (23.7% vs 4%) in the index households compared to control households (OR=7.49 [95% CI : 4.47 to 12.62]). We then asked if smoking was allowed in this room with the baby present. The numbers only slightly decreased (21.1% of the cases compared to 3.1% of the controls) whilst the associated risk between the two groups slightly increased (OR=8.42 [95% CI : 4.79 to 14.98]). Finally we asked whether smoking was allowed in **any** room where the baby was present. Nearly half the index parents (47.9%) responded that this was allowed compared to less than a quarter of the controls (21.0%). This difference was significant (OR=3.47 [95% CI : 2.46 to 4.90]).

Table 2.37 gives the dose-response effect of the number of smokers in the household (including mothers smoking after pregnancy, partners and others) in those households where smoking was allowed in any room where the baby was present.

Table 2.37 - Number of smokers in households where smoking was allowed with the infant present : dose-response effect

Number of smokers	SIDS		Controls		OR [95% CI]
	N	%	N	%	
None	101	52.3	615	80.4	1.00 [Ref Group]
1 smoker	22	11.4	66	8.6	2.44 [1.36 to 4.37]
2 smokers	59	30.6	77	10.1	5.15 [3.24 to 8.21]
3 or more smokers	15	5.7	7	0.9	10.43 [3.34 to 32.54]

N–193 SIDS & 765 Controls

Clearly, the risk to the infant increased with the number of smokers in the household.

(ii) Number of cigarettes to which the baby is exposed

Table 2.38 shows the dose-response effect, in terms of the average number of cigarettes smoked by all smokers, in just those households where smoking was allowed in the same room as the infant.

Table 2.38 - Number of cigarettes smoked in households where smoking was allowed with the infant present : dose-response effect					
Number of smokers	SIDS		Controls		OR [95% CI]
	N	%	N	%	
None	101	52.3	615	80.4	1.00 [Ref Group]
1-19 cigarettes	18	9.3	56	7.3	2.47 [1.29 to 4.73]
20 to 39 cigarettes	40	20.7	67	8.8	3.96 [2.40 to 6.55]
40 or more cigarettes	34	17.6	27	3.5	7.57 [4.00 to 14.32]
N–193 Cases & 765 Controls					

Again there was a strong dose-response effect, however we cannot assume that the infant or smoker were both present when all these cigarettes were smoked. As a proxy measure for levels of postnatal exposure this is an indirect measurement.

(iii) Parental estimate of infant's daily exposure to tobacco smoke

As a more direct proxy measure, we also asked the parents to estimate on an average day approximately how many hours the baby was exposed to a smoky atmosphere, this included exposure outside, as well as inside the household. Only 9 index parents (4.6%) replied that they did not know the number of hours of exposure and only 9 controls (1.1%). Of these 18 sets of parents, at least one parent smoked, in two-thirds both parents smoked and responded that they smoked in the same room as the baby. Results will therefore be slightly underestimated.

Over half the index babies (56.4%) were exposed to at least an hour of smoke compared to less than a quarter of the control babies (24.0%). This result was significant (OR=3.97 [95% CI : 2.73 to 5.78]). As a continuous variable, the estimated number of hours of exposure was significant ($P<0.0001$).

Table 2.39 - Parental estimation of infant's daily exposure to tobacco smoke					
Hours per day	SIDS		Controls		OR [95% CI]
	N	%	N	%	
0 hours	85	45.7	593	76.9	1.00 [Ref Group]
1-2 hours	26	14.0	90	11.7	1.99 [1.14 to 3.46]
3-5 hours	22	11.8	45	5.8	3.84 [1.97 to 7.48]
6-8 hours	19	10.2	18	2.3	6.78 [3.17 to 14.49]
> 8 hours	34	18.3	25	3.2	8.29 [4.28 to 16.05]
N–186 SIDS & 771 Controls					

Table 2.39 shows that the dose-response effect was strikingly clear, illustrating a linear

increase in risk as the daily number of hours of exposure increased.

4 Recent illness in baby

Health in the last week

The parents were asked how healthy their infant had been in the week before the last/reference sleep.

Table 2.40 - Parental estimation of infant's health in the last week					
Infant health	SIDS		Controls		OR [95% CI]
	N	%	N	%	
Good	131	67.2	582	74.8	1.00 [Ref Group]
Fair	47	24.1	158	20.3	*1.32 [0.89 to 1.95]*
Poor	17	8.7	38	4.9	1.99 [1.02 to 3.74]
As a single parameter on 2 degrees of freedom p<0.01 N=195 SIDS & 778 Controls					

A small proportion of mothers responded that the health of their child was poor in the final week, significantly more index infants compared to control infants.

Quantifying illness with a retrospective scoring system

The "Cambridge Babycheck" [178] is a scoring system to help parents and doctors quantify serious illness in babies up to 6 months of age (which includes over 80% of the babies in this study). It is based on 7 symptoms and 12 signs, each of which receives a score if they are evident, the higher the score the less well the baby. All but four of the questions (those pertaining to the direct response of the infant during the interview) have been built into the questionnaire as a "retrospective revised babycheck".

The scores are grouped and action is linked to each group :

Score 0 to 7	Baby is generally well.
Score 8 to 12	Baby is unwell but not seriously ill, get advice and observe baby
Score 13 to 19	Baby is ill and needs a doctor
Score 20+	Baby is seriously ill and needs a doctor straight away

The maximum score possible using the "Cambridge Babycheck" is 111, the maximum possible score using the revised babycheck of the questionnaire was 96. Care must therefore be taken when interpreting the revised babycheck results as these will be an underestimate of the baby's ill-health.

The details of these questions and how they are scored are given in Appendix VIII, along with a detailed analysis of the individual questions. The overall pattern suggests a small but greater proportion of the index infants scored higher for most of the individual questions. In the last 24 hours more of the SIDS infants took less fluids, passed less urine, were more drowsy, had episodes of vomiting and looked abnormally pale. Furthermore, the mother heard a more unusual cry, heard wheezing or whistling noises on the chest and thought the baby was more floppy. The analysis of individual questions however does not reveal whether the discrepancy between the two groups is due to a large proportion of SIDS infants showing a few signs and symptoms of illness, or a small group of SIDS infants showing many signs and symptoms. For this we need to analyse the composite score.

The "Cambridge Babycheck" also requires a temperature reading which could not be ascertained from these infants retrospectively. However, a proxy measure was used by asking whether the infant had had a fever *in the final week. There was no significant* difference between the SIDS infants and controls using this proxy measure. Table 2.41 gives the composite score for the revised babycheck both with and without the proxy measure for temperature.

Table 2.41 - Composite score of revised babycheck

Composite score	SIDS		Controls		OR [95% CI]
Excluding temperature	N	%	N	%	
0 to 7	156	80.4	720	92.4	1.00 [Ref Group]
8 to 12	21	10.8	23	2.9	4.50 [2.30 to 8.83]
13 to 19	8	4.1	26	3.3	}
20+	9	4.6	10	1.3	} 2.37 [1.18 to 4.76]
Including temperature	N	%	N	%	
0 to 7	147	75.8	697	89.5	1.00 [Ref Group]
8 to 12	21	10.8	41	5.3	2.76 [1.50 to 5.09]
13 to 19	15	7.7	25	3.2	}
20+	11	5.7	16	2.1	} 3.39 [1.87 to 6.17]

N=194 SIDS & 779 Controls

Looking at the scores excluding the proxy measure for temperature shows us that over

80% of the index babies and over 90% of the controls were fairly healthy. Significantly more of the index babies were unwell (score 8 to 12) but not likely to be seriously ill and significantly more index babies were ill (score 13+) and required medical treatment. Infants scoring 13 to 19, or more than 20, were added together as the numbers were small. The results were similar if we included or excluded temperature. Both revised babycheck scores were significant if treated as a continuous variable ($p<0.0001$).

Infant sweating in last 24 hours

Mothers were asked whether their infant sweated in the last 24 hours and whether this was more than usual.

Table 2.42 - Infant sweating in last 24 hours

	SIDS		Controls		OR [95% CI]
Did the baby sweat	N=193	%	N=779	%	
No	147	76.2	639	82.0	1.00 [Ref Group]
Yes	46	23.8	140	18.0	1.43 [0.95 to 2.11]
More than usual	N=193	%	N=778		
No	179	92.7	745	95.8	1.00 [Ref Group]
Yes	14	7.3	33	4.2	1.77 [0.85 to 3.47]
N=194 SIDS & 779 Controls					

Slightly more of the index infants sweated more in the last 24 hours and for slightly more of these infants this was unusual. The difference however, was not significant.

5 Bed-sharing and room-sharing

Bed-sharing

Parents were asked whether they bed-shared with their infant on the last night.

Table 2.43 - Bed-sharing

On last night :	SIDS		Controls		OR [95% CI]
At all	N	%	N	%	
No	121	66.1	538	71.7	1.00 [Ref Group]
Yes	62	33.9	212	28.3	1.30 [0.90 to 1.86]
More than an hour	N	%	N		
No	136	74.3	635	84.7	1.00 [Ref Group]
Yes	47	25.7	115	15.3	1.86 [1.23 to 2.81]
For the whole night	N	%	N	%	
No	154	84.2	719	95.9	1.00 [Ref Group]
Yes	29	15.8	31	4.1	4.12 [2.30 to 7.4]
N=183 SIDS & 750 Controls					

In 12 SIDS cases and 30 controls this was not applicable because either it was a day-time sleep or the parents were not present for the last sleep. If we include these infants as lone sleepers, the significance associated with bed-sharing for the whole night remained (OR=3.92 [95% CI : 2.20 to 6.98]). Slightly more of the index parents took their baby to bed for at least part of the night compared to the controls, but this difference was not significant. However, some of the mothers would only have taken the baby to bed for a very short period (to feed perhaps or because the baby would not settle). We therefore asked whether the parents took their baby to bed for an hour or more on the last night. Over a quarter of the index parents responded that they did so compared to 15% of control parents. This significance increased when we looked at those parents and infants that bed-shared for the whole night.

Table 2.44 shows, for those parents that bed-shared for more than an hour, the reasons as to why they did so.

Table 2.44 - Reasons for parents sharing bed with infant

Reasons	SIDS		Controls	
	N	%	N	%
Usually slept that way	17	36.2	24	20.9
Baby would not settle	13	27.7	33	28.7
To feed & fell asleep	13	27.7	41	35.7
To feed only	3	6.4	12	10.4
Baby seemed unwell	1	2.1	5	4.3

N=47 SIDS & 115 Controls

This was the usual practice for more of the index parents than controls. The majority of parents took their baby to bed because this was their usual practice, to feed the baby or because the baby would not settle. Very few parents took their baby to bed because the baby seemed unwell, proportionally more controls than cases. Looking just at the group that bed-shared for the whole night, the main reason was because this was their usual practice (51.7% SIDS vs 64.5% Controls). Again, for very few parents was it because the baby seemed unwell (3.4% of cases, 3.2% of controls). A similar proportion of both index and control infants (13.8% vs 9.7%) shared the bed with sibling(s) as well as parent(s) and a similar proportion in both groups were found adjacent to just one parent (72.4% vs 61.3%).

Finally we looked at the usual practice of bed-sharing and 26% of the index parents compared to 14.2% of the control parents took their baby to bed for more than 2 nights in any week. This difference was significant (OR=2.38 [95% CI : 1.33 to 4.27]).

<u>Room-sharing</u>

(i) Room baby was put in for sleep

Table 2.45 describes the room in which the infants slept for the usual night or day sleep and for the last/ reference sleep.

Table 2.45 - Room baby was put in for sleep

Room	Usually at night		Usually in day		Last/Ref Sleep	
	SIDS N=195 %	Controls N=779 %	SIDS N=194 %	Controls N=777 %	SIDS N=195 %	Controls N=778 %
Own bedroom	17.9	29.5	10.9	14.6	16.4	24.4
Shared bedroom	13.3	8.0	4.7	3.1	13.8	6.8
Parental bedroom	55.9	61.2	12.5	10.1	44.6	53.5
lounge	9.7	1.0	58.9	61.7	18.5	10.3
Other room	0	0.1	4.6	6.1	1.5	2.0
Only one room *	2.1	0	2.1	0	2.1	0.1
Other	1.0 [1]	0.1 [2]	6.2 [3]	4.1 [4]	3.0 [5]	2.8 [6]

* Only one room in the household ie caravan or bedsit
1 = hospital
2= office
3= outside, hospital & varied
4= outside, at nursery, office & varied
5= at nursery, in garage, in ambulance, at hospital
6= outside, in office, in car

More of the control babies had their own bedrooms or slept in the parental bedroom both usually and for the last reference sleep, whilst more of the index babies slept in a room shared by others (excluding parents) or in the lounge. A small proportion of index infants shared a room with the whole family, but this was the only room in the household. Comparing infants who shared the parental bedroom with those who did not, this was more common amongst the control infants for the usual night sleep (55.9% vs 61.2%), but was not significant (OR=0.80 [95% CI : 0.58 to 1.12]). For the last/reference sleep the difference just failed to reach significance (OR=0.71 [95% CI : 0.5 to 1.00]).

(ii) Who sleeps in the same room

Table 2.46 describes who slept in the same room as the infant for usual night and day sleeps and for the last/reference sleep.

Table 2.46 - Who shares the same bedroom						
Other room-sharers	Usually at night		Usually in day		Last/Ref Sleep	
	SIDS N=193* %	Controls N=779 %	SIDS N=193* %	Controls N=778 %	SIDS N=191* %	Controls N=779 %
Nobody	18.1	29.4	73.6	80.5	31.4	31.5
Parent(s) only	63.2	62.9	6.7	2.1	38.7	50.1
Sibling(s) only	9.3	3.7	2.1	0.8	8.4	3.1
Other relatives(s) only	0.5	0.3	0	0	0.5	0.5
Parents(s) & sibling(s)	8.4	3.6	0	0	9.4	3.6
Parent(s) & relative(s)	0.5	0.1	0	0	0	0.1
*Varied***	0	0	17.6	16.6	11.5	11.2

* 2 cases excluded from usual practice as mainly in hospital, 4 for last/reference sleep
** Infant slept downstairs, where others also sometimes slept

Approximately the same proportion of infants shared the same bedroom with just the parents for the usual night sleep. Significantly more index infants (81.9% vs 70.6%) shared their bedroom generally for this sleep (OR=1.88 [95% CI : 1.25 to 2.88]).

Most infants, as expected, would sleep alone for the usual day sleep. Some infants slept downstairs where others may sometimes take a nap at the same time, the proportions in the two groups were quite similar. A small but significant proportion of index parents slept with their infant for the usual day sleep (OR=3.44 [95% CI : 1.49 to 7.77]).

Significantly more of the control infants shared a room with just the parents for the last/reference sleep (OR=0.63 [95% CI : 0.45 to 0.88]), but this was not significant if other siblings as well as parents were included in the same room (OR=0.80 [95% CI : 0.57 to 1.11]) and the difference was unity if the data was dichotomised to infants sleeping in a room alone and those infants who shared a room with at least one member of the household (OR=1.00 [95% CI : 0.70 to 1.44]).

<u>6 Dummy use</u>

The parents were asked about usual infant practice for night and day sleeps regarding dummy use and whether the infant used a dummy for the last/ reference sleep. Figure 2.47

shows that slightly more of the control babies used dummies both day and night either often or always, but this difference was not significant.

Table 2.47 - Usual dummy use during day and night sleeps					
Infant uses a dummy:	SIDS		Controls		OR [95% CI]
Usually at night	N	%	N	%	
Never	82	42.5	314	40.3	1.00 [Ref Group]
Sometimes	51	26.4	183	23.5	1.07 [0.70 to 1.61]
Often	15	7.8	76	9.8	0.76 [0.38 to 1.41]
Always	45	23.3	206	26.4	0.84 [0.54 to 1.27]
Usually in day	N	%	N	%	
Never	71	36.8	280	36.0	1.00 [Ref Group]
Sometimes	67	34.7	240	30.8	1.10 [0.74 to 1.63]
Often	15	7.8	88	11.3	0.67 [0.34 to 1.26]
Always	40	20.7	170	21.9	0.93 [0.59 to 1.46]
N=193 SIDS & 779 controls for night sleep, 778 controls for day sleep					

However, substantially more of the control babies used dummies in their last sleep compared to the index babies.

Table 2.48 - Dummy use during last /reference sleep					
	SIDS		Controls		OR [95% CI]
For last sleep	N	%	N	%	
No	115	60.2	367	47.2	1.00 [Ref Group]
Yes	76	39.8	411	52.8	0.59 [0.42 to 0.84]
N–191 SIDS & 778 Controls					

7 Breast-feeding

Table 2.49 shows the proportion of mothers who made an attempt to breast-feed and the significance of the effect for those infants exposed to a longer period of feeding.

Table 2.49 - Ever breast-fed and the dose response effect					
	SIDS		Controls		OR [95% CI]
Ever breast-fed	N	%	N	%	
No	107	54.9	309	39.7	1.00 [Ref Group]
Yes	88	45.1	469	60.3	0.50 [0.35 to 0.71]
Dose-response	N	%	N	%	
Never breast-fed	107	54.9	309	39.7	1.00 [Ref Group]
≤1 week	11	5.6	57	7.3	0.56 [0.25 to 1.13]
> 1 week ≤4 weeks	19	9.7	85	10.9	0.65 [0.35 to 1.13]
*> 4 weeks**	58	29.7	327	42.0	0.51 [0.35 to 0.74]
* Includes 6 SIDS and 13 controls < 4 weeks but were still breast-feeding up to last/ref sleep. N=195 SIDS & 778 Controls					

Significantly more of the control mothers had breast-fed at least once compared to the index mothers. However, there was no identifiable dose-response effect, which may be partly due to the low numbers when the data was split into three categories. If, for those infants who breast-fed the longest, young infants (less than 4 weeks old) were excluded, the significance of the protective effect slightly increased (OR=0.48 [95% CI : 0.32 to 0.70]).

8 Baby's mattress

The following analysis is based on the antimony hypothesis referred to in Chapter 8, which suggested that babies may be more at risk if sleeping on integral plastic covered mattresses, if the mattresses were older and if the mattresses had been used by previous infants.

Mattress cover

In both groups the most popular usual practice was to use an integral plastic mattress cover, the second most common practice being to use no cover at all. Comparing those who used either an integral plastic cover to those who did not, significantly more of the controls adopted this practice (OR=0.35 [95% CI : 0.23 to 0.52]). If we assume that those classified as 'other impervious cover', shown in Table 2.50, were also plastic, the significance of the difference was maintained (OR=0.41 [95% CI : 0.29 to 0.59]).

Table 2.50 - Type of mattress cover : usual practice

Type of cover	SIDS		Controls	
	N	%	N	%
No cover	49	27.4	89	11.8
Fabric cover	18	10.1	63	8.3
Polythene cover added by parents	1	0.6	15	2.0
Rubber cover	7	3.9	5	0.7
Integral plastic cover	94	52.5	540	71.7
Other impervious cover	10	5.6	42	5.6

N=179 SIDS & 754 controls (4 SIDS parents & 3 controls did not answer this question, for a further 12 SIDS and 23 controls, mattress cover was not applicable)

We need however to examine what happened on the last/ reference sleep and specifically exclude those babies who slept in their parents bed for the majority of the night and those who slept on something other than a baby mattress. These infants are listed in Table 2.51.

Table 2.51 - Type of bed on which the infant slept				
Where infant slept	SIDS		Controls	
	N	%	N	%
Own cot	117	60.0	664	85.0
Sharing parental bed	41	21.4	46	5.9
Sleeping on settee or settee bed	19	9.9	25	3.2
Sleeping in convertible car seat	2	1.0	14	1.8
Sleeping in babychair/bouncy chair	0	0	11	1.4
Sleeping in pram/buggy	1	0.5	5	0.6
Sleeping in adult-type bed	5	2.6	2	0.3
Sleeping on or in arms of mother	1	0.5	5	0.6
Sleeping on beanbag	0	0	1	0.1
Sleeping on waterbed	1	0.5	0	0
Sleeping on piece of foam	0	0	1	0.1
Sleeping on floor	0	0	1	0.1
Infant in hospital	3	1.6	0	0
Infant in ambulance	1	0.5	0	0
Not stated	1	0.5	2	0.3
Those shaded were excluded from the analysis N 192 SIDS & 777 Controls				

This reduces the total number of cases to 117 (60%) and the controls to 664 (85%). Even so the results shown in Table 2.52 are similar to those shown in Table 2.50.

Table 2.52 - Type of mattress cover : for last/reference sleep				
Type of cover	SIDS		Controls	
	N	%	N	%
No cover	17	14.5	58	8.7
Fabric cover	8	6.9	53	8.0
Polythene cover added by parents	1	0.9	14	2.1
Rubber cover	3	2.6	4	0.6
Integral plastic cover	80	68.4	500	75.3
Other impervious cover	8	6.8	35	5.3
N 117 SIDS & 664 controls				

The most common practice was using an integral plastic cover, the second most common practice being to use no cover at all. Again comparing those who used either an integral or completely plastic cover to those who did not, significantly more of the controls adopted this practice (OR=0.53 [95% CI : 0.31 to 0.91]). Assuming that those classified as 'other impervious cover' were also plastic, more controls slept on plastic covered mattresses although the difference was not significant (OR=0.73 [95% CI : 0.45 to 1.21]).

Mattress age

Table 2.53 shows, for those infants that slept in a cot, the age of mattresses with a plastic cover (including other impervious cover).

Table 2.53 - Age of integral plastic-covered mattresses				
Age of mattress	SIDS		Controls	
	N	%	N	%
< 3 months	9	11.5	76	14.6
3 months - < 6 months	12	15.4	93	17.9
6 months - < 12 months	9	11.5	77	14.8
12 months - < 24 months	5	6.4	37	7.1
24 months - < 48 months	20	25.6	126	24.3
48 months or more	23	29.5	110	21.2
N 78 SIDS & 519 Controls (10 SIDS parents & 16 Controls did not know age)				

As a continuous variable the difference in age of mattress was not significant (p=0.61). Slightly more of the index infants slept on mattresses who were at least 4 years old, but this difference was not significant (OR=1.55 [95% CI : 0.87 to 2.70]).

Mattress used by previous child

Again we need only look at this question in terms of those babies who used a plastic covered baby mattress. Slightly more of the index babies slept on a mattress that had been used by at least one other child (67.4% vs 55.1%). This difference was not significant (OR=1.33 [95 % CI : 0.76 to 2.35]).

Infants were therefore if anything, at less risk if they slept on integral plastic covered mattresses, and there was no significant difference in the age or previous use of these mattresses.

9 Alcohol and illegal substance use

Maternal alcohol consumption

(i) Before pregnancy

The mother was asked how much alcohol she consumed before pregnancy in an average week. The median number of units for both index and control mothers was 1 unit per week (index range : 0 to 90 units, control range : 0 to 72 units). The results are given in Table 2.54.

Table 2.54 - Weekly maternal alcohol consumption				
Units per week	SIDS		Controls	
	N	%	N	%
Less than 1 unit	91	48.1	333	42.9
1 to 5 units	57	30.2	286	36.8
6 to 10 units	18	9.5	110	14.2
11 to 15 units	8	4.2	26	3.3
16 to 20 units	6	3.2	13	1.7
More than 20 units	9	4.8	9	1.2
N=189 SIDS & 777 Controls				

More of the index mothers drank less than one unit a week compared to the control mothers. Conversely more of the index mothers also consumed higher quantities of alcohol compared to control mothers. Of the index mothers, 12.2% drank more than 10 units per week compared to 6.2% of the control mothers. This difference was significant (OR=2.02 [95% CI : 1.14 to 3.57]). However, if the mother's weekly alcohol consumption was plotted as a continuous variable, the difference was weaker and lost significance ($p = 0.053$). This is perhaps not surprising as the effect of alcohol is not a linear relationship, rather a j-shaped curve. Proportionally more of the index mothers have drinking habits at the two extremes. Taking this into consideration, the data is perhaps better presented as in Table 2.55.

Table 2.55 - Weekly maternal alcohol consumption					
Units per week	SIDS		Controls		OR [95% CI]
	N	%	N	%	
1 to 10 units a week	75	39.7	396	50.9	1.00 [Ref Group]
Less than 1 unit	91	48.1	333	42.9	1.44 [1.01 to 2.06]
> 10 units a week	23	12.2	48	6.2	2.68 [1.46 to 4.82]
As a single parameter on 2 degrees of freedom $P<0.001$ N=189 SIDS & 777 Controls					

The evidence suggests that the usual alcohol consumption habits of the index mothers before pregnancy was slightly more extreme than that of the control mothers, in that significantly more index mothers either drank less than one unit a week or drank more than 10 units a week. For those mothers who drank more than 10 units of alcohol a week, the median number of units consumed by the index mothers was 20 units a week (inter-quartile range : 14 to 28 units), compared to 15 units consumed by the control mothers (interquartile range : 12 to 18 units).

(ii) During pregnancy

Having given the average weekly alcohol intake before pregnancy, the mothers were asked how this intake changed during pregnancy. Change in habit was asked for rather than exact units because of the difficulty of deriving a representative average which may be dependent on the stage of pregnancy. Options included less than one unit, decreased more than half, halved, decreased a little, stayed the same, increased a little and increased a lot. To analyse the response the data needs to be interpreted in terms of consumption before pregnancy (a mother whose consumption had stayed the same for instance would yield a different response depending on what the usual level of consumption was).

Table 2.56 shows that virtually all mothers who drank little or no alcohol before pregnancy did not drink alcohol during pregnancy. The majority of both index and control mothers who usually drank 1 to 10 units decreased their alcohol consumption during pregnancy (57% of index mothers and 58% of control mothers in this group changed from 1 to 10 units to no alcohol).

Table 2.56 - Change in weekly alcohol consumption during pregnancy

		SIDS		Controls	
Before pregnancy	During pregnancy	N	%	N	%
Less than 1 unit	*Stayed the same*	91	100	328	98.5
	Increased	0	0	5	1.5
	Decreased	-	-	-	-
1 to 10 units	*Stayed the same*	8	10.7	47	11.9
	Increased	1	1.3	4	1.0
	Decreased	66	88.0	345	87.1
11 units or more	*Stayed the same*	5	21.7	6	12.5
	Increased	1	4.3	1	2.0
	Decreased	17	73.9	41	85.4

NB % are specific to each category
N 189 SIDS & 777 Controls

Within the group of heavier drinkers, slightly more of the control mothers decreased their alcohol consumption compared to the index mothers. This difference was not significant (comparing those who stayed the same or increased with those who decreased p=0.4).

(iii) After pregnancy

As with during pregnancy, alcohol consumption after pregnancy was asked for in relation to consumption before pregnancy.

Table 2.57 - Change in weekly alcohol consumption after pregnancy					
		SIDS		Controls	
Before pregnancy	After pregnancy	N	%	N	%
Less than 1 unit	*Stayed the same*	86	94.5	308	92.5
	Increased	5	5.5	25	7.5
	Decreased	-	-	-	-
1 to 10 units	*Stayed the same*	18	24.0	159	40.4
	Increased	15	20.0	46	11.7
	Decreased	42	56.0	189	48.0
11 units or more	*Stayed the same*	7	30.4	10	20.8
	Increased	7	30.4	1	2.1
	Decreased	9	39.1	37	77.1
NB % are specific to each category N 189 SIDS & 775 Controls					

After pregnancy, a small proportion of mothers in both groups who usually did not drink alcohol increased their alcohol consumption. Of those mothers who drank 1 to 10 units, proportionally more of the index mothers increased their alcohol consumption. This difference was not significant (OR=1.89 [95% CI : 0.92 to 3.71]). Of those mothers who drank more than 10 units, over three quarters of the control mothers decreased their alcohol consumption compared to less than a third of the index mothers. This difference was significant (OR=5.23 [95% CI : 1.58 to 17.61]). Ignoring the 3 groups and comparing those mothers who increased their alcohol consumption from before pregnancy with those whose consumption stayed the same or decreased, the difference was not significant (OR=1.63 [95% CI : 0.97 to 2.66]).

Therefore the differences between the control and index mothers mainly concerned the heavier drinkers, where significantly more of the index mothers drank more than 11 units a week before pregnancy and significantly fewer decreased their consumption after pregnancy.

(iv) Binge drinking

Mothers were asked how many times in an average week they would consume more than

4 units of alcohol in any one session.

Table 2.58 - Binge drinking				
Consuming > 4 units a time each week	SIDS		Controls	
	N	%	N	%
Never	166	87.4	720	92.5
Once	12	6.3	51	6.6
Twice	6	3.2	6	0.8
Three or more times	6	3.2	1	0.1
N=190 SIDS & 778 Controls				

Significantly more of the index mothers had at least one session compared to the controls (OR=1.79 [95% CI : 1.03 to 3.03]). Only 7 of the control mothers had at least 2 sessions compared to 12 of the index mothers (p=0.00003).

(v) Drinking in the 24 hours before the last sleep

Proportionally more of the control mothers had 1 or 2 units of alcohol in the 24 hours before the last sleep, but more of the index mothers had 3 units or more. As a continuous variable, significantly more of the index mothers consumed alcohol (p=0.02) in this time period. As Table 2.59 shows, nearly twice as many index mothers consumed 2 units of alcohol or more compared to the control mothers (15.3% vs 8.7%). This difference was significant (OR=1.89 [95% CI : 1.13 to 3.15]).

Table 2.59 - Recent alcohol consumption of mother				
In 24 hours before last /reference sleep	SIDS		Controls	
	N	%	N	%
None	151	79.5	641	82.4
1 unit	10	5.3	69	8.9
2 units	7	3.7	33	4.2
3-4 units	13	6.8	21	2.7
5 or more units	9	4.7	14	1.8
N=190 SIDS & 778 Controls				

If 3 units or more was used as the cut-off (11.5% vs 4.5%) the associated risk was even greater (OR=2.62 [95% CI : 1.40 to 4.90]).

(vi) Overall pattern of maternal alcohol consumption

In conclusion, there was a consistent difference between the index and control mothers' alcohol consumption regarding quantity and pattern. More of the index mothers drank heavily before pregnancy; fewer of them reduced their intake after pregnancy; the mode of drinking was more akin to many units on a few occasions rather than a few units on many occasions and more of the index mothers drank larger amounts of alcohol in the 24 hours preceding the last sleep.

Alcohol consumption of partner

(i) Usual consumption

The partners were asked how much alcohol they consumed in an average week. The median number of units for the index partners was 3 units (range 0 to 68 units), the median number of units for the control partners was 3 to 4 units (range 0 to 189 units).

Table 2.60 - Weekly alcohol consumption of partner

Units per week	SIDS		Controls	
	N	%	N	%
Less than 1 unit	58	36.3	226	30.3
1 to 5 units	37	23.1	191	25.6
6 to 10 units	19	11.9	129	17.3
11 to 15 units	8	5.0	68	9.1
16 to 20 units	15	9.4	60	8.0
21 to 25 units	7	4.4	17	2.3
26 to 30 units	7	4.4	22	2.9
More than 30 units	9	5.6	33	4.4

N=160 SIDS & 746 Controls

As a continuous variable there was no difference in usual weekly alcohol consumption between the index partners and controls (p=0.9). As a dichotomous variable there was also no difference between the two groups: using 11 units or more as a cut-off (OR=1.10 [95% CI : 0.74 to 1.63]), or using 16 units or more as a cut-off (OR=1.46 [95% CI : 0.93 to 2.21]).

Table 2.61 - Weekly alcohol consumption of partner

Units per week	SIDS		Controls		OR [95% CI]
	N	%	N	%	
1 to 15 units a week	64	40.0	388	52.0	1.00 [Ref Group]
Less than 1 unit	58	36.3	226	30.3	1.76 [1.13 to 2.75]
> 15 units a week	38	23.8	132	17.7	1.81 [1.11 to 2.94]

N–160 SIDS & 746 Controls

Table 2.61 shows that there was a slight suggestion of the same non-linearity distribution clearly seen in usual maternal consumption. Slightly more of the index partners either drank virtually no alcohol or more than 16 units a week.

If the j-shaped curve is taken into account there are significant differences found between the index and control partners. Significantly more index partners either drank virtually no alcohol or more than 15 units per week.

(ii) Binge drinking

The partners were asked how many times they drank more than 4 units of alcohol in any one session during an average week.

Table 2.62 - Binge drinking				
Consuming > 4 units	SIDS		Controls	
a time each week	N	%	N	%
Never	115	70.6	503	67.0
Once	19	11.7	149	19.5
Twice	15	9.2	57	7.6
Three times	8	4.9	14	1.9
Four times	3	1.8	6	0.8
Five or more times	3	1.8	22	2.8
N 163 SIDS & 751 Controls				

More control partners drank 5 units or more in any one session compared to the index partners. More index partners had 2 or more of these sessions (17.8% vs 13.2%). This difference was not significant (OR=1.43 [95% CI : 0.87 to 2.28]).

(iii) Drinking in the 24 hours before the last sleep

As a continuous variable the alcohol consumption of the partners in the 24 hours preceding the last sleep was not significant (p=0.6673).

Table 2.63 - Recent alcohol consumption of partner				
In 24 hours before	SIDS		Controls	
last /reference sleep	N	%	N	%
None	108	72.0	527	71.8
1 unit	5	3.3	54	7.4
2 units	11	7.3	42	5.7
3-4 units	13	8.7	49	6.7
5-8 units	5	3.3	33	4.5
9 units or more	8	5.3	29	4.0
N=160 SIDS & 744 Controls				

As a dichotomous variable there were also no significant differences between the two groups whichever cut-off was used: using 2 or more units as a cut-off (OR=1.24 [95% CI : 0.80 to 1.90]), using 3 or more units as a cut-off (OR=1.08 [95% CI : 0.65 to 1.74]), or using 4 or more units as a cut-off (OR=1.20 [95% CI : 0.72 to 1.97]).

Maternal use of illegal substance

The mothers were asked whether in the year before, during or after pregnancy they had used any of the illegal substances listed in Table 2.64 on more than one occasion.

Table 2.64 - Maternal use of illegal substance

Substance	Before pregnancy		During pregnancy		After pregnancy	
	SIDS N=191 %	Controls N=778 %	SIDS N=190 %	Controls N=775 %	SIDS N=191 %	Controls N=777 %
None	83.8	94.7	91.6	98.6	91.6	97.6
Glue	0	0	0	0	0	0
Amphetamines	0.5	0.4	0	0	0	0
Barbiturates	0	0.1	0	0	0	0
Cannabis	14.1	4.6	6.8	1.0	7.3	1.9
Speed	2.6	1.3	1.1	0	0.5	0.1
LSD/ Acid	1.6	0.8	0	0.1	0	0
Cocaine / Crack	1.0	0	0.5	0	0.5	0
Ecstasy	1.0	0.5	0	0.3	0	0.4
Heroin	0	0	0	0	0	0

NB The % for each column may not add up to unity as some mothers may have used more than one drug

A much greater proportion of index mothers had used one or more of these illegal drugs compared to the control mothers before pregnancy (16.2% vs 5.3%), during pregnancy (8.4% vs 1.4%) and after pregnancy (8.4% vs 2.5%). The difference for each time period was significant (before pregnancy : OR=3.93 [95% CI : 2.18 to 7.09], during pregnancy : OR=7.05 [95% CI : 2.58 to 19.29], after pregnancy : OR=4.54 [95% CI : 1.92 to 10.71]). By far the most common drug used was cannabis.

Partner's use of illegal substance

As with the mothers, the partners were asked whether they had taken any of the same substances listed on more than one occasion.

Table 2.65 - Partner's use of illegal substance				
Substance	Before pregnancy		After pregnancy	
	SIDS %	Controls %	SIDS %	Controls %
None	78.5	93.4	82.8	95.9
Glue	0	0.1	0.6	0.1
Amphetamines	0	0.1	0	0
Barbiturates	0	0	0	0
Cannabis	12.2	4.6	10.1	3.3
Speed	2.3	0.5	3.0	0
LSD/ Acid	2.3	0.5	1.8	0.1
Cocaine / Crack	0.6	0	0	0
Ecstasy	2.9	0.5	0.6	0.1
Heroin	0.6	0.1	0.6	0.4
Other	0.6	0	0.6	0
N−172 SIDS & 755 Controls				

Many more of the index partners had tried at least one substance more than once in the year before pregnancy (21.5% vs 6.6%) and after pregnancy (17.2% vs 4.1%). The difference between the groups for these two time periods was significant (before pregnancy : OR=3.76 [95% CI : 2.21 to 6.37], after pregnancy : OR=5.35 [95% CI : 2.71 to 10.53]). Again the most common drug used was cannabis.

10 Length of time baby left unattended

Non-parental care in last 24 hours

The question was asked as to whether the baby had been in the care of someone other than the parents in the last 24 hours.

Table 2.66 - Non-parental carer in last 24 hours				
	SIDS		Controls	
Carer	N	%	N	%
Not in care of others	150	78.5	636	81.6
Grandparent	16	8.4	92	11.8
Aunt/ uncle	4	2.1	16	2.1
Sibling	2	1.0	2	0.3
Other relation	2	1.0	1	0.1
Father (if separated)	1	0.5	1	0.1
Friend	1	0.5	5	0.6
Baby-sitter	12	6.3	10	1.3
Childminder	3	1.6	8	1.0
Nursery/ playgroup	0	0	8	1.0
N=191 SIDS & 779 Controls				

Four index cases were excluded because they were in hospital during the last 24 hours. Proportionally more of the index infants were under the supervision of someone other than the parents for some part of the last 24 hours, but this difference was not significant (OR=1.22 [95% CI : 0.80 to 1.82]). Slightly more of the control infants were looked after by another relative whilst more of the index infants were looked after by a baby-sitter or childminder.

Table 2.67 - Time spent with non-parental carer in last 24 hours

	SIDS		Controls	
Time spent	N	%	N	%
Not in care of others	150	79.4	636	81.7
≤1 hour	4	2.1	18	2.3
> 1 hour ≤2 hours	10	5.3	30	3.9
> 2 hours ≤4 hours	7	3.7	40	5.1
> 4 hours ≤8 hours	7	3.7	29	3.7
> 8 hours	11	5.8	25	3.2
N 189 SIDS & 778 Controls				

Table 2.67 shows the amount of time each infant spent in the care of others in the last 24 hours. There was no obvious pattern, slightly more of the index infants spent less than 2 hours with the other carer and slightly more also spent more than 8 hours. Using 8 hours as a cut-off the difference was not significant (OR=1.86 [95% CI : 0.81 to 4.01]).

Longest sleep in previous 24 hours

In the 24 hours before the last or reference sleep, the parents were asked to recall the longest period for which their baby slept.

Table 2.68 - Longest sleep in previous 24 hours

Longest sleep	SIDS		Controls		OR [95% CI]
	N	%	N	%	
> 10 hours	33	18.0	207	26.6	1.00 [Ref Group]
> 7 ≤10 hours	49	26.8	234	30.0	1.31 [0.79 to 2.19]
> 4 ≤7 hours	53	30.0	249	32.0	1.34 [0.81 to 2.21]
≤4 hours	48	26.2	89	11.4	3.38 [1.97 to 5.82]
N=183 SIDS & 779 Controls					

The median length of sleep for the index infants (6 hours 25 mins [Inter-quartile range : 4

to 9 hours]) was shorter than for the control infants (8 hours [Inter-quartile range : 5 hours 30 mins to 10 hours 30 mins]). Significantly more of the index infants had 4 hours or less as their longest sleeping period compared to the controls.

The parents were also asked how usual this period of sleep was. A similar proportion in both groups thought this sleep to be the same as usual (SIDS : 72.1% vs controls : 72.3%). Re-calculating the odds ratio for the smaller subgroup of infants whose usual longest period of sleep was only 4 hours or less in any 24 hours, the associated risk (OR=3.30 [95% CI : 1.76 to 6.15]) was similar to that of the last 24 hours, suggesting the index infants usually slept for shorter periods of time. A similar proportion of parents in both groups thought the length of sleep in the last 24 hours was longer than usual (SIDS : 17.3 % vs controls : 16.9%) or shorter than usual (SIDS : 10.6% vs controls : 11.0%).

How many times the baby woke

The question was asked as to how many times the baby woke in the sleep previous to the last/ reference sleep.

Table 2.69 - How many times did the baby wake in previous sleep

Number of times baby woke	SIDS N	SIDS %	Controls N	Controls %	OR [95% CI]
None	66	35.7	271	35.1	1.00 [Ref Group]
1	50	27.0	249	32.3	0.82 [0.54 to 1.26]
2	51	27.6	170	22.0	1.23 [0.80 to 1.90]
3	10	5.4	44	5.7	0.93 [0.40 to 2.01]
4 or more	8	4.3	37	4.8	0.89 [0.34 to 2.06]

N=185 SIDS & 771 Controls

The number of times the baby woke was very similar for both index and control infants. The parents were asked whether this was a usual number of times. The answer was obviously dependent on the previous response. Utilising the response of the previous sleep given in Table 2.69, a unit was added to the number of times the baby woke if the parents responded that the number of times given was fewer than usual, and conversely a unit was subtracted if the parents responded that the number of times given was more than usual. Table 2.70 gives a proxy measure for the usual number of times the baby woke (If parents responded "don't know" to the question of "was this usual", then the number of times the baby woke in the previous sleep was left the same).

Table 2.70 - How many times did the baby wake usually					
Number of times	SIDS		Controls		OR [95% CI]
baby woke	N	%	N	%	
None	70	37.8	281	36.4	1.00 [Ref Group]
1	50	27.0	239	31.0	0.84 [0.55 to 1.28]
2	46	24.9	175	22.7	1.06 [0.68 to 1.63]
3	15	8.1	54	7.0	1.12 [0.55 to 2.15]
4 or more	4	2.2	22	2.9	0.73 [0.18 to 2.25]
N–185 SIDS & 771 Controls					

As we can see from this proxy measure, there was no difference between the index and control infants regarding the usual of times the baby woke during sleep.

11 Apparent life-threatening event

Two questions were asked to ascertain whether any of the infants had ever experienced an apparent life-threatening event. Firstly whether the infant had ever had *'an episode in which he or she became lifeless?'*. This was true for many more index babies (13.0% vs 3.2°o) than controls (OR=6.13 [95% CI : 3.21 to 12.14]). Of those that had experienced an episode, a similar proportion had more than one episode (41.7% SIDS vs 40.0% controls), contacted a doctor (58.3% SIDS vs 56.0%) and were taken to hospital (37.5% vs 28.0%). And secondly whether the infant had ever had *'any form of convulsion, fit, seizure or other turn in which consciousness was lost or any part of the body made abnormal movements?'*. Very few of the mothers noticed any such event (4.1% vs 1.0%), although there was a significant difference between the index and control infants (Fisher's Exact test : p–0.0063).

12 Maternal postnatal depression

The mother was asked whether she had suffered or was still suffering from postnatal depression and was further asked whether she thought either her own Health Visitor or GP were of the opinion that she had suffered from postnatal depression. The question of the severity of the depression was also taken from the Health Visitor's records.

Just under a fifth of both index and control mothers thought they had suffered or were still suffering from postnatal depression. Of these mothers, less than half thought that their

Health Visitor had recognised this problem.

Table 2.71 - Postnatal depression					
Mother suffering?	SIDS		Controls		OR [95% CI]
(Mother's opinion)	N=190	%	N=776	%	
Yes	36	18.9	133	17.1	1.13 [0.73 to 1.72]
(HV's opinion*)	N=188	%	N=748	%	
Yes	18	9.6	50	6.7	1.48 [0.79 to 2.66]
(GP's opinion*)	N=158	%	N=626	%	
Yes	16	10.1	32	5.1	2.09 [1.04 to 4.05]
From HV's record :	N=184	%	N=767	%	
None	159	86.4	672	87.6	1.00 [Ref Group]
Mild	20	10.9	89	11.6	0.95 [0.54 to 1.61]
Severe	5	2.7	6	0.8	p=0.044
* According to the mother					

Significantly more of the index mothers thought that their GP had recognised their postnatal depression compared to control mothers. Slightly more of the control mothers were recognised as having mild postnatal depression although this was not significant. A small group of mothers were recognised as having severe postnatal depression, significantly more index mothers. Of the 5 cases where severe depression was recognised, in 4 the mother and according to the mother the GP and HV had recognised the illness. For one other index mother, she did not think she had postnatal depression but was aware that the HV and GP thought she had. Of the 6 controls, for 3 the mother and according to the mother the HV and GP had recognised postnatal depression, for 2 controls the mother and HV had recognised the depression but not the GP and for one control the mother did not think she was suffering from depression and thought the GP or HV were of the same opinion.

13 Previous hospital admissions or attendances

The parents were asked whether the baby had had any other hospital attendances or admissions apart from an apparent life-threatening event and the reason for admission or attendance.

Significantly more of the index infants had had at least one admission or attendance to hospital compared to the controls (OR=1.87 [95% CI : 1.27 to 2.77]).

Table 2.72 - Hospital admission or attendance				
Reason	SIDS		Controls	
	N	%	N	%
Never attended	139	72.0	646	82.9
Followed up after SCBU	11	5.7	17	2.3
*Infections**	16	8.3	29	3.7
Surgery	7	3.7	18	2.3
Reaction to immunisation	0	0	2	0.3
Reaction to antibiotics	0	0	3	0.4
Hip problems	0	0	15	1.9
Kidney problems /tests	0	0	6	0.8
Jaundice	2	1.0	6	0.8
Heart murmur	1	0.5	6	0.8
Talipes	0	0	4	0.5
Accident	5	2.6	9	1.2
Other	12**	6.2	18***	2.4

* Includes : bronchiolitis, pneumonia, bronchopneumonia, chest infection, raised temperature, influenza, gastro-enteritis, vomiting, rash, urinary tract infection & septicaemia
** Includes : feeding problem (2), apnoeic attack, bulging fontanella, palsy, turning blue & fits and 5 stated as outpatient but details not given
*** Includes : eye problem (3), ear problem (2), colic (2), circumcision (2), sunken fontanella, pilondal sinus, circulatory problem, brain haemorrhage, scabies, constipation, observation for birthmark & observation because mother took thyroid tablets during pregnancy and 1 stated as outpatient but details not given.
N 193 SIDS & 779 Controls

Excluding the fact that the infant was in SCBU as a reason for admission to hospital, the difference between index and control babies was smaller but still significant (OR=1.72 [95% CI : 1.13 to 2.59]).

14 Previous deaths and access in emergency

Previous child deaths

Parents were asked whether any of their previous children (0 to 15 years old who survived birth) had died.

Table 2.73 - Previous infant deaths				
	Sex	*Age*	*How long ago*	*Cause of death*
SIDS families	Male	4 yrs 6mths	7 yrs	During hernia operation
	Female	6 mths	3 yrs 1 mth	SIDS
	Male	2 mths	6 yrs	SIDS
	Female	2 mths	4 yrs 2 mths	SIDS
Control families	Female	2 yrs 3 mths	1 yr 6 mths	SIDS
	Female	1 yr 6 mths	1 yr	Pneumonia
	Male	11 mths	8 yrs 11 mths	SIDS

Stillbirths, miscarriages and terminations are excluded

Of the index families 4 had a previous child who had died compared to 3 control families. The numbers were very small, but the index families had had significantly more previous child deaths compared to the control families (p=0.03). The main cause of death was SIDS. Comparing SIDS deaths only, the difference was not significant (p=0.06).

Use of telephone in emergencies

The parents were asked whether there was a working telephone in the home from which outgoing calls could be made. Nearly three times as many index families did not have a telephone in the home (41.5% vs 14.6%) compared to the control families (OR=4.19 [95% CI : 1.37 to 12.87]). If there was not a telephone, most index and control families responded that there was a pay-phone in the building or nearby in the street or possible use of a neighbours phone. However, of the index families, 3.6% had no access to a telephone within a 5 minute period compared to 1.2% of the controls. This difference was significant (p-0.025).

Use of own transport

The parents were asked whether they had use of any type of motorised private transport. Significantly more of the index families (51.8% vs 22.5%) did not have their own transport compared to the controls (OR=5.02 [95% CI : 3.36 to 7.49]). Of those parents who had use of transport, the question was asked as to how often the mother had access to the transport. Over three quarters (76.4%) of the index mothers had no transport, could not drive, or had no access to their partner's transport compared to 44.7% of the control mothers (OR=4.01 [95% CI : 2.77 to 5.88]).

15 Recent major life events

Moving accommodation in the last year

Parents were asked how many times they had moved to new accommodation in the last year. Nearly one half of the index parents had moved to new accommodation at least once in the last year (47.2% vs 19.2%) compared to less than a fifth of the controls. This difference was significant (OR=3.98 [95% CI : 2.20 to 4.88]). Regarding the number of moves, the responses ranged from none to 8 times, some not being able to remember the number of times as they were either a travelling family or moving from one bed and breakfast accommodation, refuge or friend's house to another.

Table 2.74 - Number of accommodation changes in the last year					
Number of moves	SIDS		Controls		OR [95% CI]
in the last year	N	%	N	%	
None	103	52.3	629	80.8	1.00 [Ref Group]
1	65	33.9	128	16.5	3.28 [2.20 to 4.48]
2 or more	27	13.8	21	2.7	8.77 [4.26 to 18.06]
Before the birth					
None	119	57.9	661	85.0	1.00 [Ref Group]
1	53	30.3	102	13.1	3.23 [2.09 to 4.99]
2 or more	23	11.8	15	1.9	9.87 [4.39 to 22.22]
After the birth					
None	170	87.2	737	94.7	1.00 [Ref Group]
1	19	9.7	38	4.9	p=0.0118
2 or more	6	3.1	3	0.4	p=0.0023
N 195 SIDS & 778 Controls					

Twice as many index families moved once during the last year compared to control families. The difference was much greater comparing those who moved more than once. Five times as many index families moved more than once in the last year compared to the control families.

Parents were also asked to break down the number of moves in the last year, before and after the baby was born. Approximately three quarters of the moves occurred before the baby was born. The difference between index families and controls both before and after birth were similar to the differences found overall for the last year whether comparing those that moved at least once before birth (OR=4.00 [95% CI : 2.68 to 5.98]), after birth (OR=3.19 [95% CI : 1.77 to 5.74]) or those that moved once or more.

Changes in family routine

The parents were asked whether the main carer of the baby (usually the parents) had any change in routine (a change that in any way would involve the infant) in the last 48 hours. The responses describing the change in routine are given in Table 2.75.

Table 2.75 - Changes in family routine				
Change in routine	SIDS		Controls	
	N	%	N	%
No change	155	79.5	681	87.4
Visiting friends, shopping, socialising	25	12.8	65	8.3
Receiving guests	5	2.6	16	2.1
Mother going back to work	0	0	5	0.6
Family on holiday	3	1.5	2	0.3
Just moved to new accommodation	1	0.5	1	0.1
Baby went to nursery	0	0	2	0.3
Decorators working in the house	0	0	2	0.3
Other reason	6*	3.1	5**	0.6

* "Preparing for holiday", "Locked out of house", "Baby given 3rd vaccine", "Baby had first bath", "Went to bed earlier than usual", Let friend feed baby".
** "Father in hospital, lots of different carers" "Baby left most of feed" "Mum in hospital with slipped disc" "Baby changed from cot to carrycot" "Father in hospital, disabled mother had to do more"
N 195 SIDS & 779 Controls

Nearly twice as many index carers had a change in routine (20.5% vs 12.6%) compared to the control carers. This difference was significant (OR=2.03 [95% CI : 1.27 to 3.25]). The main reason for a change in routine was going out of the home for the first time in a while, visiting friends, shopping or going out socialising. There appeared to be no obvious differences between the index and control carers regarding the reason for a change in routine.

Part III

Multivariable results

Chapter 12

Selecting variables for the multivariable analysis

Correlation between variables

In epidemiological studies, some lifestyle characteristics cannot be quantified by any single variable whilst other characteristics may be equally represented by several variables. Postnatal infant exposure to tobacco smoke for instance may be measured by the number of smokers in the household, the number of cigarettes smoked or a parental estimate of the number of hours exposed. The associated risk of these variables may be independent of each other and separate from the risk of exposure during pregnancy or highly correlated. There were several socio-economic markers used in this study, all significant in the univariable analysis, but difficult to pick out one definitive measure. Asking for the weekly family income gives us some idea of economic status but is only a snapshot of the family finance and does not take into account the weekly out-goings or long-term debts and savings. In the UK, social class coding based on occupation is often used as a marker in epidemiological studies along with parental education. However, in the present climate the tenure of occupation is not as secure, short-term contracts and part-time work are more common whilst academic achievement no longer guarantees a vocation that leads to a comfortable lifestyle. These measures are a proxy for socio-economic status that try and quantify deprivation. Each may measure a different facet or approximate the same thing.

As a preliminary exercise it is therefore important to look at the correlation between some of these variables to investigate whether one particular variable of the several available can be used as a proxy measure to represent a certain factor.

Comparison of socio-economic markers

Three of the socio-economic markers significant in the univariable analysis were weekly family income, parental occupation and parental education. To measure the association between these three variables the first step was to look at the correlation between them. As the variables were ordinal rather than continuous, Spearman's rank correlation coefficient was used. Table 3.1, shows the correlation coefficients for each pair of variables.

Table 3.1 - Spearman's correlation coefficients			
Correlation of markers	SIDS	Controls	Both
Social class vs family income	0.37	0.43	0.45
Social class vs parental education	0.45	0.55	0.55
Family income vs parental education	0.38	0.42	0.44
P<0.000001 for each comparison			

As the p-value shows, the strength of these coefficient values were very significant. The coefficients ranged between 0.37 to 0.55 and showed some degree of linear association, but interpretation is limited. A measure of the strength of linear association is not the same as a measure of agreement. It is possible to have a high degree of correlation when the agreement is poor. The different categories of each variable may not have a one-to-one relationship with each other. Dichotomising these variables as shown in Table 3.2, using various cut-offs, the amount of agreement was measured.

Table 3.2 - Measure of agreement			
Social Class Cut-Off	Family Income Cut-Off	Parental Education Cut-Off	Agreement %
III m, IV, V, unem.	*< £200*	-	63.5
III m, IV, V, unem.	*< £100*	-	55.8
III m, IV, V, unem.	-	*< 'O' level*	62.8
III m, IV, V, unem.	-	*< 'A' level*	70.1
-	*< £200*	*< 'A' level*	67.3
-	*< £100*	*< 'O' level*	69.5

If the agreement was very high between 2 variables then it could be argued that these two variables were measuring the same thing. However, the amount of agreement between any two of these variables ranged between 55% and 70%. There was perhaps not enough evidence here to suggest using only one of these variables as a proxy for the other two.

A further test was to stratify each of these 3 variables with the other two and use the Mantel-Haenszel test for homogeneity to see if the differences between the cases and controls were consistent across each strata. Using education for example as the variable to be stratified, Table 3.3 gives the Mantel-Haenszel results in terms of whether there were any significant differences in social class or income between the SIDS families and controls within the differently educated groups. If parental education was to be used as a proxy for the other two markers, one would expect the vast proportion of both SIDS and control families on low income or low social class to fall into the poorly educated group and that the difference between the SIDS families and controls would be non-significant at each level of educational achievement.

Table 3.3 - Mantel-Haenszel test for homogeneity

Parental education	Low social class*					Low Family Income**				
	SIDS		Controls		***	SIDS		Controls		***
	N	%	N	%	p-value	N	%	N	%	p-value
Degree/ Further Ed	18	16.7	179	12.8	<0.005	18	38.9	182	20.9	<0.25
'A'/'O' Level	87	72.4	371	53.6	<0.005	88	70.5	373	48.9	<0.001
< 'O' Level/None	84	84.5	212	76.9	<0.25	83	89.2	212	71.2	<0.001

* (IIIm, IV, V, Unemployed)
** < £200 a week
*** measuring the difference between the two groups within strata
NB N is the total number in the strata the % are the proportion of N that are low social class/ income

Clearly this was not the case, a Mantel-Haenszel test for homogeneity showed that both occupational classification ($p<0.001$) and family income ($p<0.001$) were independent of parental education.

An alternative comparative test was to put each of these three markers in the same model, using conditional logistic regression to account for the age-matching. If one marker could be used as a proxy for the other two then only one of the variables would remain significant in the model. However results showed that social class and family income were independent of each other whilst parental education remained significant with each of these variables separately but became non-significant when all three variables were in the same model ($p=0.34$).

A further proxy measure significant in the univariable analysis was receipt of Income Support (IS). A means-tested family benefit given to parents on low income. This variable was highly correlated with weekly family income and when both were put into a model, receipt of IS remained significant (OR=5.54 [95% CI : 3.29 to 9.33]) whilst weekly family income became non-significant (p=0.30), receipt of IS, like weekly family income, was also independent of occupational classification and parental education as a marker for socio-economic deprivation.

In conclusion, there was some evidence that parental education as a marker for socio-economic status could be explained by social occupational classification and family income but no clear evidence that one of these markers could be used a proxy measure for the other two. As each of these variables could also either confound or interact with other univariable findings, all three would be used in the multivariable analysis as independent variables. For occupational classification, the higher parental status was used and previous occupation was taken into account so that the unemployed group could be included in the classification. Similarly for education, the highest qualification of either parent was used. For family income, receipt of IS was used.

Comparison of factors measuring tobacco smoke exposure

The univariable analysis showed maternal smoking during pregnancy to be significantly associated with SIDS. This analysis also demonstrated other sources of exposure, from the partner, from others in the household and using a parental estimate of infant exposure as a postnatal measure. It was not clear however, if these different sources of exposure were independent risk factors or markers for maternal smoking during pregnancy. To investigate whether the univariable risks of paternal smoking and others smoking in the household were independent of maternal smoking, a two-factor analysis was conducted. Here, maternal smoking during pregnancy was used, but maternal smoking before or after pregnancy yielded similar results. Table 3.4 shows that in those households where the mother did not smoke during pregnancy but either the partner or others in the household smoked, the risk was still significant. Where both the mother smoked during pregnancy and the partner or others smoked in the household the risk was greatest.

Table 3.4 - Paternal & others smoking controlled for maternal smoking during pregnancy						
Maternal smoking during pregnancy	Paternal smoking in the household	SIDS		Controls		OR [95% CI]
		N	%	N	%	
Non-smoker	*Non-smoker*	33	16.9	421	54.0	1.00 [Ref Group]
Non-smoker	*Smoker*	40	20.5	163	20.9	3.41 [1.98, 5.88]
Smoker	*Non-smoker*	44	22.6	77	9.9	7.01 [3.91, 12.56]
Smoker	*Smoker*	78	40.0	119	15.3	8.41 [5.08, 13.92]
Maternal smoking during pregnancy	Others smoking (excluding parents)	SIDS		Controls		OR [95% CI]
		N	%	N	%	
Non-smoker	*Non-smoker*	65	33.3	561	71.9	1.00 [Ref Group]
Non-smoker	*Smoker*	8	4.1	23	2.9	p=0.007†
Smoker	*Non-smoker*	102	52.3	173	22.2	6.01 [4.12, 8.78]
Smoker	*Smoker*	20	10.3	23	2.9	7.27 [3.46, 14.94]
† Using Fisher's Exact Test						

This analysis demonstrated that paternal smoking and others smoking in the household were both independent of the risk of maternal smoking and additive in that the risk increased if both partners smoked.

Controlling the parental estimate of the infant's daily exposure to smoke, using no exposure versus any, for maternal smoking during pregnancy, the estimate of exposure also showed an independent and additive effect.

Table 3.5 - Parental estimate of exposure controlled for maternal smoking during pregnancy						
Maternal smoking during pregnancy	Parental estimate of exposure	SIDS		Controls		OR [95% CI]
		N	%	N	%	
Non-smoker	*None*	47	25.3	507	65.8	1.00 [Ref Group]
Non-smoker	*Some*	24	12.9	73	9.5	3.57 [1.91 to 6.68]
Smoker	*None*	38	20.4	86	11.2	4.43 [2.59 to 7.62]
Smoker	*Some*	77	41.4	105	13.6	7.14 [4.46 to 11.43]
N 186 SIDS & 771 Controls						

Parental estimate of postnatal exposure remained significant in those families where the mother did not smoke during pregnancy and the greatest risk was associated with exposure to both factors. Similar results were obtained using maternal smoking after pregnancy.

Therefore, the associated risk of smoking comes from several sources that were independent of each other. In the multivariable analysis, maternal smoking during or after pregnancy were used, along with variables for paternal smoking, others smoking and parental estimation of postnatal exposure to tobacco smoke.

Comparison of other factors

Some factors in the univariable analysis were looked at in different ways yielding several findings with small but significant results. Some of these findings were correlated with each other and became non-significant when entered into a multivariable model together. These findings included :

(i) Caribbean maternal ethnicity and non-white partners became non-significant when modelled with mothers and fathers of European (non-UK) origin. The latter two variables were therefore used in the multivariable analysis.

(ii) Maternal anxiety over infant's thermal environment became non-significant when either factors representing the heating being on for the duration of the sleep or the tog values of infant bedding and covering were added. The latter two variables were used in the multivariable analysis.

(iii) Maternal alcohol consumption of more than 4 units in any one session (binge drinking) and increased consumption amongst the heavier drinkers after pregnancy became non-significant when the factor representing the usual maternal alcohol consumption was added. This latter variable was used in the multivariable analysis.

(iv) Postnatal depression in terms of the GP's opinion (according to the mother) became non-significant when the factor representing severe postnatal depression noted by the Health Visitor was added to the model. This latter variable was used in the multivariable analysis.

(v) Maternal access to private transport became non-significant when the variable representing family ownership of transport was added to the model. Again this latter variable was used in the multivariable analysis.

All remaining variables significant in the univariable analysis were included in the multivariable analysis.

Variables excluded from the analysis

The criteria for exclusion was set out before the analysis began. The variables excluded fell into three main categories :

(i) Variables with no control data or for which controls were matched

Seasonality, day of death, time found dead.

(ii) Variables excluded as they were not significant in the univariable analysis

Location of parental home, place of birth, parental age difference, number of previous miscarriages, stillbirths and terminations, support from grandparents, other family and friends, infant sweating in the last 24 hours, type of mattress cover, mattress age and previous use, non-parental care in the last 24 hours, the number of times the baby woke in the previous sleep, infant congenital abnormalities, room-sharing, whether the baby had a hot water bottle or an electric blanket and whether the window or door was open in the infant's bedroom for the last sleep.

(iii) Variables initially excluded because of too many missing values

The details of these variables are given in Table 3.6.

Table 3.6 - Variables excluded because of too many missing values

Variable	Number missing			Non-Ref Group or units used	OR [95% CI]
	Case	Con	%		
Council Tax Band	79	217	30.4	Band A	3.48 [1.85 to 6.56]****
Partner's age	28	21	5.0	per 10 year unit	1.72 [1.23 to 2.42]**
Time between pregnancies	53	274	33.5	per 5 year unit	2.30 [1.29 to 4.10]**
Usual paternal alcohol consumption	35	34	7.1	No alcohol	1.76 [1.13 to 2.75]*
				>15 units	1.81 [1.11 to 2.94]*

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

For single mothers, questions regarding the partner such as age and specific alcohol consumption had to be treated as missing because the information was not available, however, for simple yes/no responses such as for smoking and drug abuse, the response was treated as 'no' rather than missing as the infant was not exposed to these factors. The time between pregnancies obviously excluded first time mothers and therefore many missing values. Unfortunately many families were not aware of their council tax band as this was a relatively new rating system. This variable is perhaps another alternative proxy measure for socio-economic status for future studies.

These variables were excluded from the initial modelling process but were tested after specific models were derived.

Variables included in the analysis

Epidemiological characteristics included

There are certain characteristics and epidemiological features common to SIDS found in many previous studies. These variables differ from the other risk factors in that they are not as amenable to change but need to be taken into account in the multivariable analysis. Some of the temporal factors mentioned above have already been matched upon and so cannot be included in the analysis. Other characteristics investigated fell into 4 main areas :

(i) Baby factors - sex, gestation, birthweight centile.
(ii) Maternal factors - number of children, multiple births, previous deaths.
(iii) Family factors - parental ages, marital status, racial/ethnic group.
(iv) Socio-economic factors - income, occupation, education, housing situation.

Table 3.7 gives the details of those epidemiological factors that were significant in the univariable analysis.

Table 3.7 - Epidemiological characteristics included in the analysis

Variable	**Number missing**			**Non-Ref Group or units used**	**OR [95% CI]**
	Case	Con	%		
Birthweight centiles	5	15	2.1	per 2 standard dev.	2.53 [1.76 to 3.63]****
Damp in baby's room	2	2	0.4	Yes	1.82 [1.06 to 3.14]*
European (not UK) mother	0	0	0	Yes	2.99 [1.03 to 8.28]*
Gestational age	4	14	1.8	per 4 week unit	2.63 [1.94 to 3.58]****
Highest parental education	2	4	0.6	< 'A' Level	2.46 [1.62 to 3.72]****
Marital status	0	0	0	Single	5.05 [2.73 to 9.35]****
Maternal age	0	0	0	per 10 year unit	2.76 [1.92 to 3.97]****
Multiple births	0	0	0	Twin/Triplet	14.31 [3.92 to 52.14]****
Number of children	0	0	0	per 1 child unit	1.56 [1.35 to 1.81]****
No. of people per room	1	2	0.3	per person a room	5.08 [2.95 to 8.74]****
Occupational classification	3	14	1.7	IIIm, IV,V,Un	2.63 [1.79 to 3.89]****
Previous infant deaths	1	8	0.9	Yes	7.33 [1.50 to 35.75]*
Receipt of IS	1	3	0.4	Yes	6.27 [4.15 to 9.47]****
Sex	0	0	0	Male	1.52 [1.09 to 2.12]*
Tenure of accommodation	0	1	0.1	Rented	4.19 [2.86 to 6.13]****

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

All of the characteristics mentioned in the four groups above were significant. Paternal age was significant but was excluded at this stage because of too many missing values. The 15 variables above were used in the multivariable analysis.

Risk factors included

All the factors listed in Table 3.8 were significant in the univariable analysis and therefore were included in the multivariable analysis.

Table 3.8 - Factors included in the analysis

Variable	Number missing			Non-Ref Group or units used	Univariable OR [95% CI] adjusted for age
	Case	Con	%		
Attempted breast-feeding	0	2	0.2	Ever	0.50 [0.35 to 0.71]****
Baby admitted to SCBU	3	10	1.3	Yes	3.97 [2.47 to 6.37]****
Bed-sharing all of last sleep	0	0	0	Yes	3.92 [2.20 to 6.98]****
Bed-sharing usually	0	0	0	Yes	2.38 [1.33 to 4.27]***
Change in routine last 24hrs	0	1	0.1	Yes	2.03 [1.27 to 3.25]**
Dummy used for last sleep	4	2	0.6	Yes	0.59 [0.42 to 0.84]**
Episode of lifelessness	3	1	0.4	Yes	6.13 [3.21 to 12.14]****
Episode of convulsion/ fit	2	1	0.3	Yes	5.68 [1.93 to 16.70]**
Family no access to phone	2	6	0.8	More than 5 mins	4.19 [1.37 to 12.87]*
Family with no transport	0	1	0.1	Yes	5.02 [3.36 to 7.49]****
Head covered when found	15	13	2.9	Yes	18.93 [7.64 to 46.90]****
Heating on for all last sleep	7	8	1.5	Yes	2.14 [1.30 to 3.50]**
Length of previous sleep	12	1	1.3	< 5 hours	2.80 [1.74 to 4.50]****
Loose bed-covers last sleep	10	6	1.6	Yes	2.72 [1.11 to 6.65]*
Mat drug abuse after preg	4	3	0.7	Yes	4.54 [1.92 to 10.71]***
Mat drug abuse during preg	5	5	1.0	Yes	7.05 [2.58 to 19.29]****
Mat smoking after preg	0	0	0	Yes	5.19 [3.57 to 7.55]****
Mat smoking during preg	0	0	0	Yes	4.84 [3.33 to 7.04]****
Moving house	0	2	0.2	Once in last year	3.28 [2.20 to 4.48]****
	-	-	-	More than once	8.77 [4.26 to 18.06]****
Moving house after the birth	0	2	0.2	Yes	3.19 [1.77 to 5.74]****
Moving house before birth	0	2	0.2	Yes	4.00 [2.68 to 5.98]****
Others smoking in househld.	0	0	0	Yes	2.99 [1.71 to 5.25]****
Neonatal problems	3	10	1.3	Yes	2.51 [1.61 to 3.91]****
Pat drug abuse before birth	0	0	0	Yes	3.76 [2.21 to 6.37]****
Pat drug abuse after birth	0	0	0	Yes	5.35 [2.71 to 10.53]****
Paternal smoking	0	0	0	Yes	3.04 [2.13 to 4.13]****
Postnatal depression	11	13	2.5	Severe	5.09 [1.27 to 20.41]*
Postnatal exposure to smoke	9	9	1.8	per 6 hour unit	2.57 [1.95 to 3.37]****
Previous hosp. admissions	12	1	1.3	Yes	1.87 [1.27 to 2.77]**
Recent mat alc consumption	5	2	0.7	> 2 units	2.62 [1.50 to 4.90]**
Resuscitation at delivery	5	13	1.8	Intubation/CPR	6.04 [2.64 to 13.81]****
Revised babycheck score	1	1	0.2	per 10 points score	2.22 [1.64 to 3.01]****
Sleeping position put down	7	6	1.3	Side	2.01 [1.38 to 2.93]***
at time of death/ref sleep	-	-	-	Front	9.58 [4.86 to 18.87]****
Sleeping position put down	0	0	0	Side	1.63 [1.13 to 2.35]**
usually	-	-	-	Front	6.29 [3.19 to 12.40]****
Tog value when put down	4	1	0.5	per 4 tog units	1.67 [1.32 to 2.11]****
Tog value for usual sleep	2	1	0.3	per 4 tog units	1.51 [1.19 to 1.92]***
Using a duvet for last sleep	1	1	0.2	Yes	2.82 [1.95 to 4.08]****
Usual mat alc consumption	6	3	0.9	> 10 Units a week	2.02 [1.14 to 3.57]*
Wore hat at time put down	3	1	0.4	Yes	4.02 [1.28 to 12.62]*

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

Chapter 13

Results of the multivariable models

The multivariable models were constructed in three different ways. Firstly a two stage empirical model where the epidemiological factors were tested first and then the rest of the variables significant in the univariable analysis were added. The second was based on a temporal structure, looking at the associated risk factors of SIDS as a sequence of events from conception, through pregnancy, labour and delivery, the infants life and the period just before death. Finally a series of models were constructed based around the specific infant environments involving those factors found to be significant in the empirical and temporal models. Variables with a large number of missing values were tested after the stepwise procedure for each model.

Odds ratios and p-values are quoted for all variables. For ease of reading, rather that any statistical convention, significant factors in each table are listed in ascending order, the most significant first, non-significant variables (OR & p-value the result of adding that variable to the remaining significant variables) are shaded and also listed in ascending order. The proportion of subjects remaining in each model is quoted below the results.

<u>The empirical two stage model</u>

Table 3.9 shows the epidemiological features that remained significant.

Table 3.9 - Significant epidemiological features

Variable	OR [95% CI]	p-value
Receipt of Income Support	3.48 [2.08 to 5.84]	$p<0.0001$
Maternal age	3.10 [1.87 to 5.15]	$p<0.0001$
Birthweight adjusted for sex & gestation	2.54 [1.60 to 4.04]	$p<0.0001$
Gestational age	2.17 [1.51 to 3.12]	$p<0.0001$
Number of children	1.96 [1.57 to 2.45]	$p<0.0001$
Multiple births	11.38 [2.04 to 63.55]	$p=0.006$
Marital status	2.95 [1.30 to 6.68]	$p=0.01$
Occupational classification	1.55 [0.95 to 2.55]	$p=0.08$
European (not UK) mothers	3.12 [0.72 to 13.56]	$p=0.13$
Sex	1.35 [0.88 to 2.07]	$p=0.17$
Tenure of accommodation	1.35 [0.80 to 2.42]	$p=0.26$
Previous infant deaths	3.32 [0.36 to 30.53]	$p=0.29$
Damp/mould in baby's room	1.25 [0.62 to 2.53]	$p=0.53$
Number of people per room	1.18 [0.57 to 2.44]	$p=0.66$
Highest parental education	0.94 [0.54 to 1.63]	$p=0.81$

Model includes 97.7% of cases and controls

Highly significant factors included young mothers, larger families, families in receipt of Income Support and infants with shorter gestation and lower birthweight. Receipt of Income Support explained more of the variation between the two groups than other socio-economic deprivation markers such as low social class, poor education, insecure tenure of accommodation and overcrowding or housing problems that especially affected the infant's room. Single mothers and multiple births were also significant epidemiological factors. Sex of the infant, country of maternal birth and previous infant deaths were not significant when the other variables were taken into account.

Adding those epidemiological variables with many missing values neither paternal age nor the council tax band of the accommodation were significant but the continuous variable representing the time between pregnancies remained in the model, suggesting the time between pregnancies was much shorter for SIDS mothers. However, for over a third of all mothers, this pregnancy was the first, the result of therefore adding the time between consecutive pregnancies would be to exclude a third of the data. An alternative way of representing the time between pregnancies, as indicated in the univariable analysis, would be to use a dichotomous variable, setting the interval between pregnancies at less than 7 months. Mothers for whom this pregnancy was the first could then be included in the reference group of mothers where the interval was 7 months or greater. This would over-estimate any difference between the two groups as a larger proportion of control mothers (41.4%) had just one pregnancy compared to SIDS mothers (25.6%). However, adding this alternative dichotomous variable representing the short time between pregnancies was not significant when added to the rest of the significant factors (OR=1.74 [95% CI : 0.88 to 3.43]).

Table 3.10 shows the resultant model when those risk factors amenable to change are added. Receipt of Income Support, marital status and multiple births, significant in the first stage, become non-significant when the remaining variables were added. The variables listed in Table 3.8 that do not appear in Table 3.10 were also not significant. Adding each of those variables that had several missing values, paternal age, time between pregnancies and the council tax band of the accommodation did not affect the model, paternal weekly alcohol consumption was also not significant.

Table 3.10 - Significant factors in the Empirical model				
	Full empirical model		Excluding '*Head covering*'	
Variable	OR [95% CI]	p-value	OR [95% CI]	p-value
Head covered when found	37.30 [7.07, 196.76]	<0.0001	-	-
Number of children	2.41 [1.72, 3.38]	<0.0001	2.26 [1.67, 3.05]	<0.0001
Dummy for last sleep	0.25 [0.12, 0.51]	0.0002	0.35 [0.18, 0.67]	0.001
Gestational age	2.97 [1.68, 5.23]	0.0002	2.29 [1.40, 3.75]	<0.0001
Maternal age	4.12 [1.91, 8.88]	0.0003	4.45 [2.19, 9.06]	<0.0001
Put down prone for last sleep	9.32 [2.49, 34.97]	0.0009†	7.61 [2.31, 25.08]	0.0009‡
Episode of lifelessness	8.47 [2.31, 31.01]	0.001	7.81 [2.39, 25.58]	0.0007
Birthweight adj for sex and gest	2.65 [1.41, 5.00]	0.003	2.99 [1.64, 5.47]	0.0004
Postnatal exposure to smoke	2.14 [1.30, 3.52]	0.003	1.83 [1.17, 2.87]	0.009
Moving house (once in last year)	3.28 [1.45, 7.40]	0.004††	4.00 [1.90, 8.40]	0.0003‡‡
Change in routine in last 24 hrs	4.71 [1.59, 13.94]	0.005	2.50 [1.03, 6.06]	0.04
Bed-sharing all of last sleep	4.91 [1.26, 19.10]	0.02	3.31 [1.05, 10.39]	0.04
Usual maternal alcl consumption	5.62 [1.63, 19.38]	0.03	4.75 [1.50, 15.05]	0.008
Revised babycheck score	2.08 [1.10, 3.95]	0.03	2.22 [1.28, 3.84]	0.004
Paternal drug abuse	5.75 [1.06, 31.02]	0.04	4.74 [1.17, 19.21]	0.03
Put down side pos. (last sleep)	1.73 [0.87 to 0.22]	0.12†	2.00 [1.06, 3.79]	0.03‡
Receipt of Income Support	1.85 [0.85 to 4.04]	0.12	2.02 [0.99 to 4.08]	0.05
Moving house (more than once)	2.88 [0.54 to 15.40]	0.22††	2.01 [0.53 to 7.56]	0.30‡‡
Multiple births	3.85 [0.17 to 86.62]	0.40	3.28 [0.13 to 79.60]	0.47
Marital status	1.75 [0.47 to 6.58]	0.41	2.67 [0.79 to 9.03]	0.11

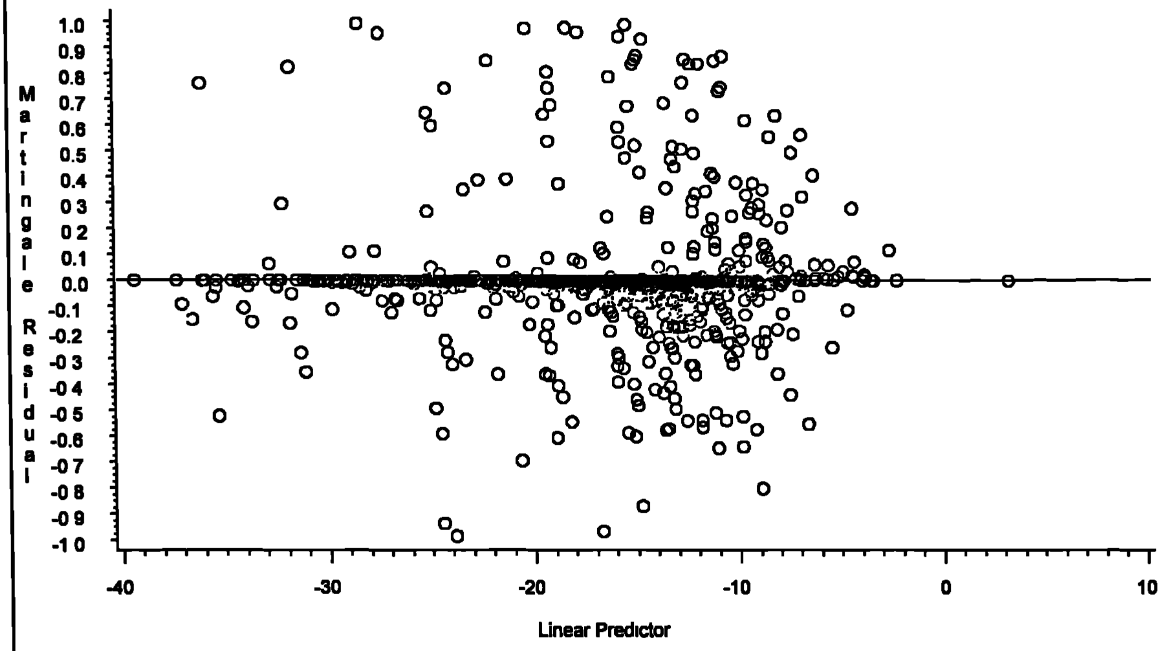
† Likelihood Ratio Test for sleeping position put down for last/ref sleep: p<0.001
‡ Likelihood Ratio Test for sleeping position put down for last/ref sleep: p<0.001
†† Likelihood Ratio Test for moving house: p<0.025
‡‡ Likelihood Ratio Test for moving house: p<0.001
Full empirical model includes 90.2% of cases and controls, second model includes 92.1%

The resultant empirical model showed that infants found with the covers over their heads were at considerably increased risk. This observation, though present in nearly a fifth (18.7%) of SIDS victims, was rare in control infants (2.4%) and in the multivariable analysis was found to have the largest associated risk. This factor is unique amongst those included in the analysis in that it relates to events which occur **after** the infant has been put down to sleep and, for this reason, the multivariable analysis was conducted with this factor included and with it excluded. Excluding head covering and repeating the multivariate analysis again, a virtually identical model was derived. The same variables remained significant, none of the previously tested variables became significant when added to this new model except for those infants put down in the side position. The multi-categorical variables of sleeping position and moving house both achieved overall significance when considered as a single parameter using the Likelihood Ratio Test.

Testing how well the empirical model fits the resultant residual plot is shown in Figure

3.1. There were no obvious outliers, nearly 80% of the residuals lay on or near to zero, suggesting there was no lack of fit of the model to individual observations.

Figure 3.1 - Martingale Residual Plot



However, interpretation of the empirical model is difficult. For instance, receipt of Income Support could be interchanged with maternal alcohol consumption to produce an equally valid model, similarly with maternal and paternal smoking for postnatal exposure to smoke and admission to SCBU instead of gestational age. Furthermore, some variables are strongly associated with other variables, low birthweight for maternal smoking during pregnancy for instance, whilst others lie just outside the 5% significance level. Quoting the resultant odds ratios from the above model would underestimate the true multivariable odds ratio as the model is over-fitted for any one outcome. Given these difficulties there is some important information from this empirical model :

(i) The main areas of significance appear to be the sleeping environment, disruption of the household, recent health of the infant and parental use of drugs, alcohol and cigarettes. These areas require further investigation.

(ii) The variables representing maternal age, gestational age, number of children, prone sleeping and found with covers over the head were highly significant.

(iii) The possible protective effect of dummies and the associated risk of the infant being put down on their side, also found in a recent New Zealand study [121], are relatively new findings and need further investigation.

(iv) Bed-sharing for more than an hour on the last night remains significant in the multivariable model and requires further investigation.

(v) Possible markers for low-socio economic status such as tobacco exposure, alcohol consumption and dummy use remain in the model whilst strong proxy measures such as family income and receipt of Income Supplement do not. The interaction between proxy measures of socio-economic status and factors associated with them need to be investigated.

(v) Many variables, although significant in the univariable analysis, lose their significance in the multivariable model. For some variables this was because the difference between the two groups was relatively small, for others the variables remaining in the model equally explained the differences and these variables could be interchanged. Some variables however are notable for their exclusion, especially those variables representing the thermal environment and intention to breast-feed.

The temporal model

Table 3.11 shows those variables that were significant around the time of conception.

Table 3.11 - Significant variables at conception

Variable	OR [95% CI]	p-value
Maternal age	3.79 [2.34 to 6.14]	<0.0001
Receipt of Income Support	2.65 [1.63 to 4.30]	<0.0001
Number of children	1.90 [1.54 to 2.33]	<0.0001
Family not got own transport	1.91 [1.18 to 3.10]	0.008
Marital status	2.43 [1.15 to 5.13]	0.02
Occupational classification	1.32 [0.82 to 2.11]	0.26
European (not UK) mothers	2.01 [0.52 to 7.72]	0.31
Not having a telephone	1.94 [0.51 to 7.30]	0.33
Previous infant deaths	2.74 [0.32 to 23.50]	0.36
Parental education	1.24 [0.74 to 2.09]	0.43
Tenure of accommodation	1.13 [0.69 to 1.84]	0.62
Model includes 99.6% of cases and controls		

Highly significant variables included young single mothers, larger families and socio-economic deprivation measured by both receipt of family income and not having any transportation. Variables that were non-significant include further measures of socio-economic deprivation, previous infant deaths and country of maternal birth. Adding those variables with several missing values relevant to the time of conception; paternal age, the council tax band of the property and the time between pregnancies did not affect the model.

Given the significant variables found above, the next stage was to add all the variables relevant to the period during pregnancy. Table 3.12 shows those variables that remained significant when added to the model in Table 3.11. The risk associated with not having transportation becomes non-significant at this stage, otherwise the significant variables mentioned above, remain significant in this second model. Further important variables now include maternal smoking during pregnancy, paternal smoking and families who had moved house at least once before the birth. Usual maternal alcohol consumption and parental drug abuse during pregnancy were not significant factors. Adding usual paternal alcohol consumption as a variable with several missing values did not affect the model.

Table 3.12 - Adding significant variables during pregnancy

Variable	OR [95% CI]	p-value
Moving house before the birth	2.64 [1.60 to 4.36]	<0.0001
Number of children	1.83 [1.48 to 2.26]	<0.0001
Maternal age	2.57 [1.55 to 4.25]	0.0003
Paternal smoking	2.22 [1.40 to 3.51]	0.0006
Receipt of Income Support	2.35 [1.43 to 3.86]	0.0007
Marital status	4.08 [1.80 to 9.27]	0.0008
Maternal smoking during pregnancy	1.82 [1.16 to 2.87]	0.01
Family not got own transport	1.61 [0.96 to 2.70]	0.07
Paternal drug abuse before birth	1.82 [0.93 to 3.56]	0.08
Maternal drug abuse during pregnancy	2.89 [0.86 to 9.72]	0.09
Usual maternal alcohol consumption	1.46 [0.68 to 3.13]	0.33
Model includes 99.5% of cases and controls		

Note that the significance of marital status increased which may be due some confounding between this variable and the variable representing lack of transportation which just dropped out of the model, single mothers being less likely to have sufficient funds for their own transportation. Note also that paternal smoking was actually more significant than maternal smoking during pregnancy.

The next stage was to add variables around the time of delivery to the above model.

Table 3.13 - Adding significant variables around delivery		
Variable	OR [95% CI]	p-value
Moving house before the birth	3.79 [2.13 to 6.74]	<0.0001
Number of children	1.93 [1.53 to 2.44]	<0.0001
Receipt of Income Support	2.83 [1.64 to 4.88]	0.0002
Paternal smoking	2.53 [1.53 to 4.19]	0.0003
Multiple births	26.36 [3.61 to 192.60]	0.001
Maternal age	2.40 [1.38 to 4.15]	0.002
Marital status	4.08 [1.64 to 10.33]	0.003
Birthweight adjusted for sex and gestation	2.01 [1.21 to 3.32]	0.007
Gestational age	1.70 [1.06 to 2.72]	0.03
Baby admitted to SCBU	2.34 [1.01 to 5.40]	0.047
Sex	1.55 [0.98 to 2.45]	0.06
Maternal smoking during pregnancy	1.50 [0.90 to 3.50]	0.12
Neonatal problems	1.57 [0.74 to 3.34]	0.24
Resuscitation at delivery	1.38 [0.32 to 6.03]	0.67
Model includes 97.3% of cases and controls		

Low birthweight, shorter gestational age, admission to SCBU and multiple births became significant factors. The large odds ratio of the latter variable should be qualified by the wide confidence interval suggesting multiple births was a significant risk factor but the numbers were very low. The significance of gestational age and admission to SCBU weakened when both variables were in the model, suggesting there was some confounding perhaps because pre-term infants were more likely to be taken for observation. Maternal smoking during pregnancy became non-significant, but was interchangeable with low birthweight, a known outcome of smoking during pregnancy, whilst paternal smoking remained significant. Infant gender just failed to reach significance and both variables representing the type of resuscitation at delivery and neonatal problems, although significant in the univariable analysis, were not significant in this model.

Table 3.14 shows the significant variables when postnatal factors were added to the above model. Gestational age disappeared from the model but admission to SCBU became much more significant. Maternal smoking after pregnancy was highly correlated with maternal smoking during pregnancy which was confounded by low birthweight, hence its non-significance, whilst paternal smoking remained in the model and postnatal exposure became a new significant factor.

Table 3.14 - Adding significant postnatal variables

Variable	OR [95% CI]	p-values
Moving house before the birth	3.86 [2.05 to 7.28]	<0.0001
Baby admitted to SCBU	3.79 [1.79 to 8.05]	<0.0001
Number of children	1.72 [1.35 to 2.20]	<0.0001
Usually put down prone	5.57 [1.80 to 17.21]	0.002†
Receipt of Income Support	2.40 [1.31 to 4.43]	0.003
Maternal age	2.59 [1.59 to 4.18]	0.006
Multiple births	23.15 [2.24 to 239.17]	0.01
Episode of lifelessness	4.15 [1.44 to 12.00]	0.01
Birthweight adjusted for sex and gestation	2.14 [1.20 to 3.81]	0.01
Paternal drug abuse after birth	3.78 [1.25 to 11.39]	0.02
Paternal smoking	1.99 [1.14 to 3.47]	0.02
Marital status	3.37 [1.20 to 9.43]	0.04
Post-natal exposure to smoke	1.53 [1.03 to 2.14]	0.048
Gestational age	1.60 [0.98 to 2.61]	0.05
Length of previous sleep	1.91 [0.94 to 3.91]	0.08
Tog value for usual sleep	1.36 [0.77 to 2.40]	0.26
Attempted breast-feeding	0.72 [0.40 to 1.29]	0.28
Maternal drug abuse after pregnancy	1.98 [0.49 to 8.02]	0.34
Moving house after the birth	1.51 [0.57 to 4.01]	0.41
Episode of convulsion/fit	1.93 [0.39 to 9.55]	0.42
Post-natal depression	2.15 [0.30 to 15.51]	0.45
Number of people per room	1.36 [0.55 to 3.34]	0.51
Others smoking in the household	1.33 [0.50 to 3.48]	0.57
Damp/ mould in baby's room	1.26 [0.54 to 2.92]	0.59
Bed-sharing usually	1.16 [0.41 to 3.21]	0.78
Previous hospital admissions	1.01 [0.54 to 1.90]	0.98
Maternal smoking after pregnancy	1.00 [0.54 to 1.87]	0.99
Usually put down on side	1.00 [0.57 to 1.77]	0.99†

† Likelihood Ratio Test for usual sleeping position : p<0.01
Model includes 93.6% of cases and controls

Other postnatal factors that became significant included those infants usually put down in the prone position, those infants that had an apparent life-threatening event and paternal drug abuse after birth. There was no risk associated with infants who usually slept in the side-sleeping position, although when side and prone position were considered as a single parameter the risk associated with this factor was significant. Notably, attempt to breast-feed, usual bed-sharing with parents, moving house after the birth and the fact SIDS infants were usually wrapped warmer were not significant factors.

Finally, adding those variables concerning the events around the time of death/ reference sleep, Table 3.15 shows that sleeping position on the last night was more significant than usual sleeping position which became non-significant. Both marital status and multiple births also became non-significant. Infants found with a cover over their head again carried a very high risk. Removing this variable from the model, factors for side-sleeping, using a duvet, loose bed-covering and the revised babycheck score became almost but not quite significant. Other significant variables around the time of death included the possible protective effect of using a dummy, bed-sharing with parents for the whole night and a change in the carer's routine in the previous 24 hours.

Table 3.15 - Adding variables around time of last/ reference sleep
The final temporal model

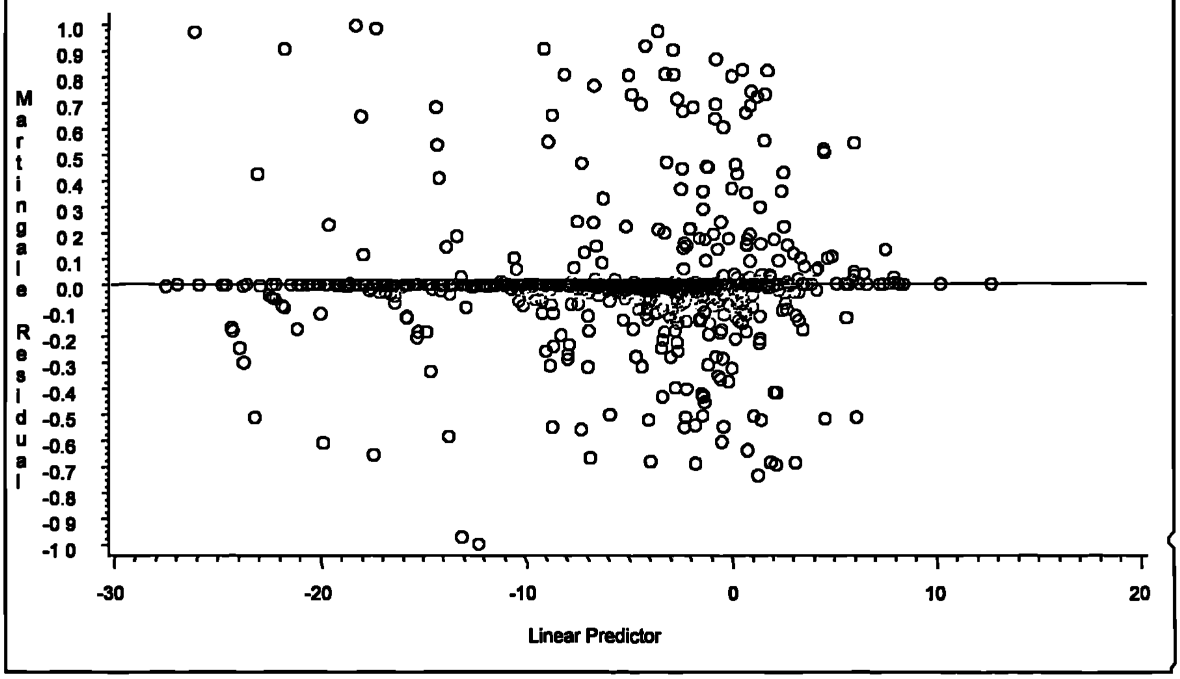
Variable	OR [95% CI]	p-value	OR [95% CI]	p-value
Found with covers over head	22.20 [5.32, 92.68]	<0.0001	-	-
Dummy used for last sleep	0.25 [0.12, 0.50]	<0.0001	0.32 [0.26, 0.38]	0.0003
Number of children	2.05 [1.56, 2.84]	<0.0001	1.96 [1.50, 2.63]	<0.0001
Baby admitted to SCBU	4.78 [2.05, 11.16]	0.001	4.69 [2.12, 10.36]	0.0006
Put down prone for last sleep	6.88 [1.99, 23.75]	0.002†	8.19 [2.66, 25.21]	0.001‡
Episode of lifelessness	5.85 [1.81, 18.88]	0.004	5.56 [1.95, 15.88]	0.002
Change in routine last 24 hrs	4.57 [1.66, 12.57]	0.005	3.14 [1.33, 7.38]	0.01
Maternal age	2.89 [1.72, 4.93]	0.005	2.84 [1.70, 4.91]	0.001
Receipt of Income Support	2.79 [1.33, 5.85]	0.007	2.79 [1.41, 5.52]	0.003
Moving house before the birth	2.86 [1.31, 6.25]	0.01	3.10 [1.51, 6.39]	0.0002
Postnatal exposure to smoke	1.85 [1.36, 2.62]	0.01	1.69 [1.21, 2.40]	0.02
Paternal drug abuse after birth	5.86 [1.24, 27.70]	0.02	5.38 [1.47, 19.69]	0.01
Bed-sharing all of last sleep	4.88 [1.28, 18.32]	0.02	3.06 [1.04, 8.95]	0.04
Paternal smoking	2.25 [1.15, 4.43]	0.02	2.06 [1.12, 3.77]	0.03
Birthweight adj for sex and ges	1.95 [1.03, 3.70]	0.04	2.14 [1.23, 3.76]	0.01
Usually put down on side	3.65 [0.98 to 11.60]	0.05††	3.42 [0.94 to 10.50]	0.07‡‡
Revised babycheck score	1.85 [0.99 to 3.47]	0.06	1.83 [0.98 to 3.43]	0.06
Usually put down prone	17.54 [0.64 to 479.46]	0.09††	10.98 [0.40 to 300.41]	0.16‡‡
Multiple births	7.77 [0.72 to 83.58]	0.09	8.52 [0.83 to 86.84]	0.07
Put down on side for last sleep	1.71 [0.88 to 3.33]	0.12†	1.77 [0.95 to 3.30]	0.07‡
Marital status	2.34 [0.68 to 8.01]	0.18	2.22 [0.71 to 6.96]	0.17
Using a duvet for last sleep	1.63 [0.80 to 3.34]	0.18	1.69 [0.90 to 3.20]	0.11
Wore hat at time put down	8.20 [0.20 to 336.34]	0.27	4.76 [0.27 to 87.67]	0.28
Tog values when put down	1.12 [0.79 to 1.81]	0.37	1.19 [0.89 to 2.01]	0.09
Loose bed-covers for last sleep	1.69 [0.27 to 10.52]	0.57	1.73 [0.36 to 8.24]	0.49
Heating on for all last sleep	1.31 [0.48 to 3.52]	0.60	1.10 [0.45 to 2.70]	0.83

† Likelihood Ratio Test for sleeping position put down for last/reference sleep: $p<0.001$
‡ Likelihood Ratio Test for sleeping position put down for last/reference sleep: $p<0.001$
†† Likelihood Ratio Test for usual sleeping position: $0.1>p>0.05$
‡‡ Likelihood Ratio Test for usual sleeping position: $0.1>p>0.05$
Full temporal model includes 90.2% of cases and controls, the second model contains 92.1%

The final temporal model was very similar to the empirical model. Regarding epidemiological features; young mothers and larger families were consistent highly significant factors, short gestation, whether measured by age or admission to SCBU remained in both models as did low birthweight. Low socio-economic status, represented by receipt of Income Support remained a significant factor throughout the sequence of events, for the empirical model this factor could be interchanged with maternal alcohol consumption. Maternal smoking during pregnancy was confounded with low birthweight but smoking in terms of parental estimates of postnatal exposure remained in the both models. Prone-sleeping for the last/ reference sleep was a highly significant risk factor in both models, side-sleeping was significant in the empirical model but just failed to reach significance in the temporal model. The overall risk associated with these two dummy variables was significant in both models but not significant for the usual sleep. The risk associated with infants being found with covers over their head remained highly significant. How normal and healthy the SIDS infants actually were is questionable given that some of these infants suffered at least one episode of lifelessness and recent health measured by the revised babycheck was significant in the empirical model and only just failed to remain in the temporal model. Family disruption also seemed to play its part both in terms of moving house, particularly before birth, and a change in routine before the last sleep. Bed-sharing and dummy use were not significant in terms of their usual practice, but rather for the last/reference sleep, a temporal anomaly that needs to be explored.

Not surprisingly, the resultant residual plot of the temporal model, shown in Figure 3.2, was similar to the empirical model in that there were no obvious outliers and nearly 80% of the residuals lay on or near to zero, suggesting there was no lack of fit of the model to individual observations.

Figure 3.2 - Martingale Residual Plot



Specific models

Sleeping & thermal environment

A whole host of factors pertaining to the infant's sleeping and thermal environment were found to be significant in the univariable analysis. Some factors such as prone-sleeping position and bed-sharing were also found to be significant in previous studies. Other factors appear to be emerging as further new risk factors such as the lateral sleeping position and infants being found with their heads covered or a protective factor such as using a dummy during sleep. Some variables, significant in previous studies, were not significant in the multivariable modelling, notably thermal environment and breast-feeding. The empirical and temporal models, controlling for all variables, were over-fitted and could not properly assess the impact of these findings. The significance is more accurately measured by considering a model that controls specifically for those variables associated with the sleeping and heating environment and then adding other significant factors, found in the empirical and temporal models, that may be potential confounders. The results are presented in Table 3.16.

Table 3.16 - Multivariable analysis of sleeping and thermal environment factors				
	Just sleeping environment factors		Full multivariable model*	
Variable	OR [95% CI]	p-value	OR [95% CI]	p-value
Put down prone for last sleep	10.03 [4.33, 23.23]	<0.0001†	9.00 [2.84, 28.47]	0.0003‡
Put down on side for last sleep	2.16 [1.36, 3.43]	0.001†	1.84 [1.02, 3.31]	0.04‡
Head covered when found	31.38 [10.36, 95.00]	<0.0001	21.58 [6.21, 74.99]	<0.0001
Tog values when put down	1.02 [0.72, 1.45]	0.90	1.00 [0.65, 1.53]	0.99
Wore hat at time put down	6.21 [0.74, 51.93]	0.09	3.82 [0.19, 78.80]	0.4
Heating on for all last sleep	3.14 [1.60, 6.17]	0.0009	1.99 [0.78, 5.69]	0.15
Attempted breast-feeding	0.42 [0.26, 0.67]	0.0003	0.99 [0.51, 1.92]	0.97
Bed-sharing all of last sleep	4.06 [1.78, 9.23]	0.0008	4.36 [1.59, 11.95]	0.008
Dummy used for last sleep	0.44 [0.27, 0.70]	0.0005	0.38 [0.21, 0.70]	0.001
Used a duvet for last sleep	1.88 [1.14, 3.12]	0.01	1.72 [0.90, 3.30]	0.12
Loose bed covering for last sleep	1.40 [0.33, 2.73]	0.70	1.73 [0.31, 9.51]	0.53

* Controlling for maternal age, number of children, gestation, birthweight, receipt of Income Support, change in routine, revised babycheck, exposure to tobacco smoke and the sleeping environment factors that remained significant.

† Likelihood Ratio Test for sleeping position put down for the last/ref sleep : p<0.001

‡ Likelihood Ratio Test for sleeping position put down for the last/ref sleep : p<0.001

First model includes 94.9% of cases and controls, the second 92 3%.

Using this more specific model, factors relating to the thermal environment still appear to be less significant than results from previous studies. Although SIDS infants were wrapped slightly warmer and a small but significant proportion wore hats, these factors were not significant when other factors relating to the sleeping environment were taken into account. More of the SIDS infants slept in rooms where the heating was on for the whole of the sleep, but this again was not significant when other risk factors were taken into account. Breast-feeding was not significant when controlled for other factors.

The five important factors that emerged in the sleeping and thermal environment did not concern usual practice but the circumstances at the time of last/ reference sleep. These include putting infants down prone or on their side, sharing the parental bed, infants not using a dummy and infants found with their heads covered.

Are these factors significant for all families or are certain families more at risk than others? Tables 3.17 and 3.18 stratify sleeping position and dummy use for three proxy measures of socio-economic status. The numbers are too small to perform a similar stratification for infants that bed-shared or were found with covers over their head, but using cruder cut-offs suggest similar results to below.

Table 3.17 - Sleeping position put down stratified by socio-economic markers							
Socio-economic markers	SIDS			Controls			Within stratum p-value
Social Class :	N	% Side	% Prone	N	% Side	% Prone	
I,II,IIIN	50	34.0	14.0	375	25.6	3.7	p<0.005
IIIM,IV	99	45.5	17.2	341	36.4	2.6	p<0.001
V, Unemployed	36	36.1	13.9	44	34.0	2.3	p<0.25
Family Income :	N	% Side	% Prone	N	% Side	% Prone	
£200+	44	38.6	15.9	395	24.6	3.3	p<0.001
£100 - <£200	60	38.3	20.0	212	35.4	1.9	p<0.001
<£100	81	43.2	12.3	158	41.1	4.4	p<0.1
Receipt of IS :	N	% Side	% Prone	N	% Side	% Prone	
No	64	40.6	17.2	554	29.1	2.9	p<0.001
Yes	123	41.5	14.6	218	36.7	3.7	p<0.001
Mantel-Haenszel pooled test across strata for all 3 socio-economic factors is significant (p<0.001)							

Regardless of which socio-economic measure is used, there does not appear to be a preferred sleeping position amongst the different social groupings. The significant difference between SIDS and control infants was maintained across each strata suggesting the risk associated with these positions was not higher for any particular group.

Table 3.18 - Dummy use on last sleep stratified by socio-economic markers					
	SIDS		Controls		Within stratum p-value
Social Class :	N	% dummy	N	% dummy	
I,II,IIIN	51	33.3	378	46.8	p < 0.1
IIIM,IV	102	42.2	343	58.6	p < 0.005
V, Unemployed	35	42.9	43	65.1	p < 0.1
Family Income :	N	% dummy	N	% dummy	
£200+	44	34.1	397	48.9	p<0.1
£100 - <£200	62	37.1	214	57.9	p<0.01
<£100	82	45.1	158	55.7	p<0.25
Receipt of IS :	N	% dummy	N	% dummy	
No	64	31.3	558	52.0	p<0.05
Yes	126	44.4	218	55.0	p<0.1
Mantel-Haenszel pooled test across strata for all 3 factors is significant (p<0.001)					

Each of these 3 socio-economic markers showed dummy use on the last sleep to be slightly more common in the lower social stratum, however, the difference in proportion between the SIDS and control groups was maintained across all strata. This suggests the effect associated with dummy use was significant regardless of socio-economic status.

Surprisingly, there was no difference in the **usual** practice of dummy use between SIDS infants and controls. Table 3.19 calculates the separate risks associated with those infants who usually use a dummy and those who used a dummy for the last/reference sleep.

Table 3.19 : Usual use of dummy compared to use on last sleep						
		SIDS		Controls		OR [95% CI]
Usually†	Last Sleep	N	%	N	%	
No	*No*	61	31.9	236	30.3	1.00 [Ref Group]
Yes	*No*	54	28.3	131	16.8	1.59 [1.02 to 2.49]
No	*Yes*	5	2.6	30	3.9	0.64 [0.19 to 1.78]
Yes	*Yes*	71	37.2	381	49.0	0.72 [0.49 to 1.07]

† For day and night sleeps only
N–181 SIDS & 778 Controls

The protective effect of dummies used for the last/reference sleep does not reach significance when split amongst those infants who usually had a dummy or usually did not. However, subdividing in this manner is bound to reduce significance. The important observation from this table is the significant risk associated with those infants who usually use a dummy, but did not use one for the last/reference sleep. Interpretation of these findings is therefore difficult as dummies could be seen as protective, as more control infants used them for the last sleep, but could also be seen as a risk if , once the habit has been initiated, it was not continued.

The risk associated with both infants found with covers over their head and bed-sharing were not confounded by socio-economic status, but further investigation of the latter variable suggests the risk cannot be generalised to the whole population. More of the index mothers had consumed 3 or more units of alcohol in the preceding 24 hours (44.8%) compared to the control mothers (19.3%), the risk associated with bed-sharing was higher amongst those that consumed alcohol although bed-sharing was still significant amongst those who did not consume alcohol (OR=2.92 [95% CI : 1.44 to 5.87]). Most of the index mothers who bed-shared also smoked (86.2% vs 35.5%). If bed-sharing was adjusted for maternal smoking after pregnancy the risk associated with bed-sharing became non-significant for non-smokers (OR=2.55 [95% CI : 0.80 to 8.19]), in this group, twice as many control infants shared the parental bed compared to SIDS infants (5.2% SIDS vs 10.0% controls). However, the risk of bed-sharing remained highly significant for mothers who smoked (OR=17.57 [95% CI : 7.58 to 40.72]). If bed-sharing was split into these two groups in the overall model, the significance of this result remained (multivariable OR for bed-sharing amongst non-smokers =2.27 [95% CI : 0.41 to 12.54] and multivariable OR for bed-sharing amongst smokers =9.25 [95% CI : [2.51 to 34.02]). Clearly the results suggest that bed-sharing is a significant risk amongst mothers who smoke but it is not clear, because of the low numbers, whether bed-sharing is a risk amongst non-smokers. If an interaction term representing mothers who smoke and bed-share is utilised, maternal smoking remains significant (OR=5.06 [95% CI: 3.32 to 7.71]), bed-sharing becomes non-significant (OR=2.89 [95% CI : 0.88 to 9.41]) but the interaction term is also non-significant (OR=1.25 [95% CI : 0.30 to 5.21], p=0.62). However, the non-smoking bed-sharing group consists of only 4 index mothers.

Exposure to tobacco smoke

Many previous studies have established an association between maternal smoking during pregnancy and SIDS. However, the strength of this association is difficult to ascertain as several risk factors associated with SIDS such as young maternal age, low socio-economic status, alcohol consumption and drug abuse are also associated with mothers who smoke. If maternal smoking during pregnancy was just a marker for these other factors then its significance would be lost when all these factors are put together. Table 3.20 gives the results for such a model.

Table 3.20 - Multivariable analysis of exposure to tobacco smoke		
Variable	OR [95% CI]	p-value
Put down prone for last sleep	5.83 [2.42, 14.06]	<0.0001†
Maternal age	3.25 [1.84 to 5.74]	<0.0001
Gestational age	2.14 [1.45 to 3.16]	<0.0001
Number of children	1.83 [1.44 to 2.33]	<0.0001
Bed-sharing all of last sleep	3.32 [1.47, 7.48]	0.0004
Receipt of Income Support	2.25 [1.29, 3.91]	0.0004
Maternal smoking during pregnancy	**1.96 [1.17, 3.28]**	**0.01**
Paternal drug abuse	3.44 [1.17, 10.11]	0.02
Usual maternal alcohol consumption	2.51 [1.16 to 5.43]	0.02
Marital status	2.89 [1.12, 7.43]	0.03
Put down in side position for last sleep	1.64 [0.94 to 2.71]	0.06†
Maternal drug abuse	1.72 [0.39 to 7.65]	0.48
Attempt to breast-feed	1.01 [0.61 to 1.67]	0.97

† Likelihood Ratio Test for sleeping position put down for the last/ref sleep : p<0.001
Model includes 94.4% of cases and controls

Controlling for many confounders maternal smoking during pregnancy remained significant. Results from this study further suggest that the risk from tobacco exposure was not limited to smoking during pregnancy. Adding further variables to the model that represent tobacco exposure such as paternal smoking, others smoking in the household and parental estimate of infant's daily exposure to smoke, both maternal smoking during pregnancy and others smoking in the household became non-significant but paternal smoking (OR=2.37 [95% CI : 1.37 to 4.10]) and parental estimate of exposure (OR=1.48 [95% CI : 1.04 to 2.12]) remained significant. This was perhaps not surprising because of the partial correlation within the four variables, and reduction in significance because of certain confounders. A closer investigation of confounding effects was therefore undertaken.

As already mentioned, there has been a shift of SIDS families to the lower socio-economic group, a group where the incidence of smoking is higher, suggesting a possible confounding effect. There were several markers used for socio-economic status in this study. Adjusting maternal smoking during pregnancy in the above model using a combination of these markers, only receipt of Income Support remained in the model and decreased the effect of smoking, although smoking remained significant. Table 3.21 shows the significance associated with maternal smoking during pregnancy when stratified for three of these markers.

Table 3.21 - Maternal smoking during pregnancy stratified by socio-economic markers					
Socio-economic marker	SIDS		Controls		Within strata p-value
Social Class :	N	% Smoked	N	% Smoked	
I,II,IIIN	52	40.3	378	18.8	p < 0.001
IIIM,IV	103	68.0	343	28.3	p < 0.001
V, Unemployed	37	81.1	45	51.1	p < 0.01
Family Income :	N	% Smoked	N	% Smoked	
£200+	46	43.4	397	16.9	p<0.001
£100 - <£200	62	59.7	214	30.8	p<0.001
<£100	82	74.4	159	37.7	p<0.001
Receipt of IS :	N	% Smoked	N	% Smoked	
No	66	34.8	558	19.0	p<0.001
Yes	128	76.6	219	40.6	p<0.005
Mantel-Haenszel test for homogeneity for all 3 factors is significant (p<0.001)					

Stratifying for maternal smoking during pregnancy, the incidence of smoking, as expected, increased in the lower social strata. However, the risk associated with smoking was maintained in each stratum level for all 3 socio-economic variables, the Mantel-Haenszel test for homogeneity was strongly significant (P<0.001) suggesting that the associated risk cannot be explained by any differences in the social groupings.

An alternative analysis was to retrospectively match for socio-economic status and calculate the resultant risk of maternal smoking during pregnancy. Choosing just one control for each index infant, matched as closely as possible in terms of parental occupation, 60.9% matched exactly and a further 23.4% within one classification. The resultant odds ratio was still highly significant (OR=3.50 [95% CI : 2.17 to 5.66]). Similar results were obtained when using parental income, receipt of Income Support and parental educational achievement.

Significantly more of the index mothers consumed greater amounts of alcohol than the control mothers on a weekly basis. As alcohol consumption and smoking are related there may be a confounding effect. Table 3.22 stratifies maternal smoking during pregnancy by weekly maternal alcohol consumption.

Table 3.22 - Maternal smoking during pregnancy stratified by alcohol consumption					
Weekly maternal alcohol consumption	SIDS		Controls		Within strata p-value
	N	% Smoked	N	% Smoked	
0 Units	93	57.0	330	27.9	p < 0.001
1-10 Units	73	61.6	400	22.0	p < 0.001
> 10 Units	23	78.3	30	50.0	p < 0.1
Mantel-Haenszel test for homogeneity is significant (p<0.001)					

As expected, the incidence of smoking increased with the heavier consumption of alcohol. However, the difference between the two groups remained constant in each strata, low numbers accounting for the failure to achieve significance in the last group. The overall test for homogeneity was highly significant. Similar results were obtained when stratified for maternal illegal drug use.

Clearly infant exposure to tobacco smoke was a highly significant risk factor when controlled for all other relevant factors, independent of socio-economic status and alcohol consumption. The source of exposure is not just from mothers smoking during pregnancy. Paternal smoking and infant postnatal exposure measured by parental estimation were independent of maternal smoking during pregnancy in the univariable analysis and remained significant in the multivariable models.

Part IV

Changes in epidemiology & risk factors

Chapter 14

Comparison of epidemiological features pre and post 1991

Features that have remained the same

Comparing the results from this study with previous studies many of the epidemiological features that characterise SIDS infants and families have remained the same, despite the recent fall in SIDS incidence.

As with the findings from previous studies discussed in Chapter 4, the age distribution peaked at 14 weeks with very few deaths in the first 4 weeks of life or after 6 months of age. Findings from this study confirm that SIDS was more prevalent in males and these infants had a lower birthweight and shorter gestation. Most deaths occurred unobserved during night-time sleep, confirming the early findings by Bergman [66] and Froggatt [58] whilst the peak daily incidence of SIDS on Thursday and Friday was in line with Fedrick [61] and McGlashan [94], although the finding from the current study was not significant. Like previous studies there was a strong correlation with young maternal age and higher parity and the risk increased with multiple births.

Some of the previous studies have looked at interactions between these common epidemiological features, such as maternal age and parity, and further inter-relationships between these features and specific risk factors such as sleeping position amongst boys and girls and birthweights of infants exposed to tobacco smoke during pregnancy. Findings from this study confirm the relationships found in these studies.

Many of the SIDS infants were born into larger families where the mother tended to be younger compared to the control infants. Controlling for many other factors, both young maternal age and larger families proved to be strong epidemiological features of SIDS both in previous studies [64, 101, 106, 114, 149, 150] and this one. The following four figures compare the age of the mothers given the size of the family; one child, two children, three children and four or more.

Figure 4.1 - One child families : Maternal age comparison

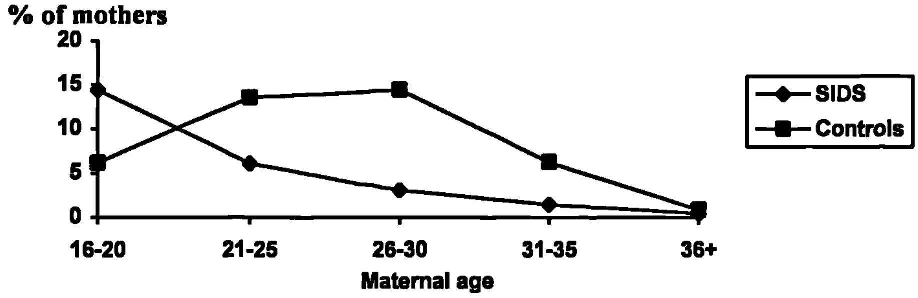


Figure 4.2 - Two children families : Maternal age comparison

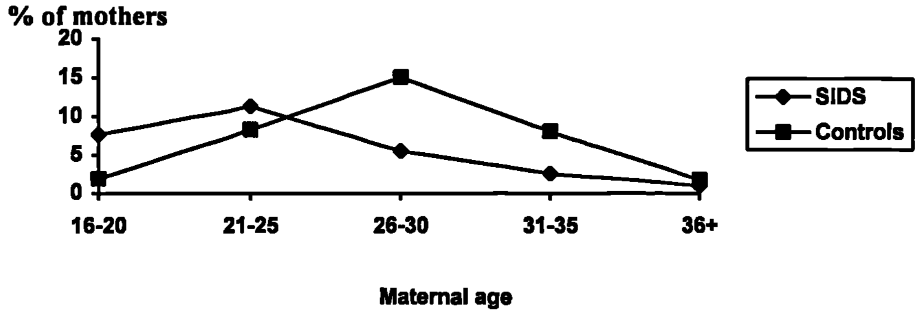


Figure 4.3 - Three-children families : Maternal age comparison

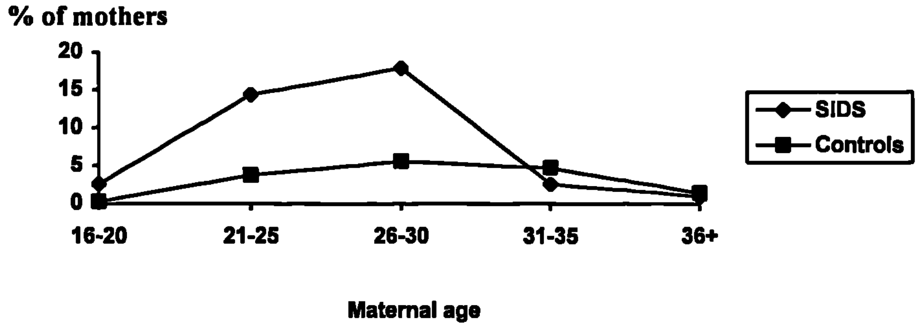
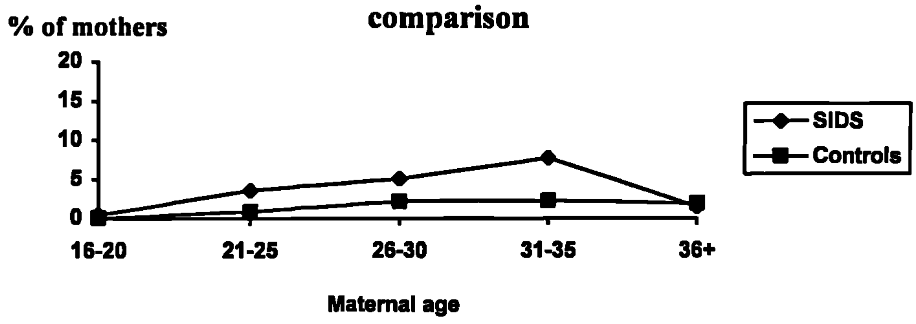


Figure 4.4 - Four + children families : Maternal age comparison



The differences between the groups in Figures 4.1 to 4.4 are not explained by a large proportion of young SIDS mothers with large families, rather the difference in age is constant as the size of the family grows. For each additional child the proportion of younger mothers remains higher for an additional age-group. This explains why both maternal age and the number of children remain not just significant in each model but also independent. Thus a characteristic feature of mothers of SIDS infants is that they started having children at an earlier age and the number of subsequent births came at similar or shorter intervals to the infants born to the older control mothers.

There was still a slight predominance of males (60%) in this study, similar to the mean proportion of males calculated for the 45 studies where gender was reported. National surveys in the Netherlands [179] between 1985 and 1991 showed that more boys than girls were placed in the prone sleeping position. Table 4.1 shows data from this study regarding sleeping position stratified for gender.

Table 4.1 - Sleeping position stratified for gender

Sleeping position:	SIDS		Controls		Within strata p-value
put down	N	% boys	N	% boys	
Supine	82	54.9	509	50.3	$p > 0.5$
Side	74	64.9	241	49.4	$p < 0.05$
Prone	30	66.7	24	66.7	$p=1.0$
found					
Supine	67	53.7	618	50.3	$p>0.5$
Side	43	51.2	82	44.6	$p>0.5$
Prone	77	68.8	45	62.2	$p>0.5$

N are the total number in each strata, the % is the proportion of boys

The Mantel-Haenszel test for homogeneity was not significant suggesting these two variables were not independent and that gender played a part in the sleeping position of infants. Amongst the SIDS more of the boys slept in the prone position, however this was also true for the control infants, the exact same proportion of infants put prone were boys. However, significantly more of the index infants put down to sleep on their side were boys and more boys than girls rolled from side to prone. The risk associated with male infants became non-significant when both factors were put in the same model (OR=1.40 [95% CI : 0.98 to 1.99]). These results suggest that part of the gender difference may be explained by the position in which the infants were put down.

Male infants are usually heavier at birth yet despite a predominance of males, the SIDS infants in this study were of lower birthweight. This discrepancy was not explained when short gestational age was taken into account. However, low birthweight is a known outcome of maternal smoking during pregnancy. Because so many of the index mothers smoked, this may have accounted for part or all of the reason as to why index infants had significantly lower birthweights.

Figure 4.5 - Birthweight Z-score for mothers who smoke

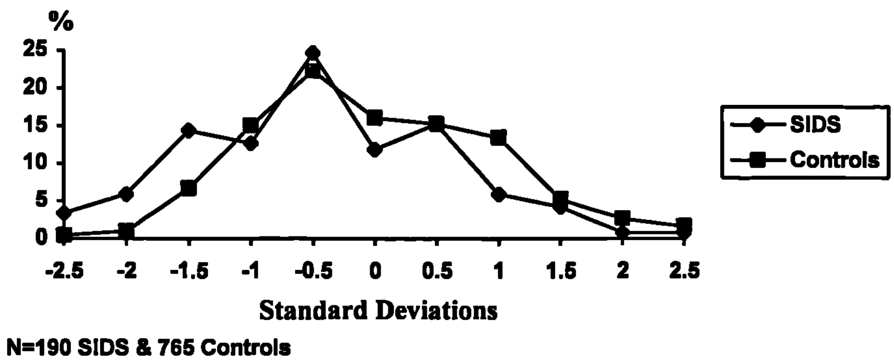


Figure 4.5 shows the distribution of birthweight adjusted for sex and gestational age for those infants whose mothers smoked during pregnancy. The difference between the index infants and controls was still significant (p=0.001).

Figure 4.6 - Birthweight Z-score for mothers who do not smoke

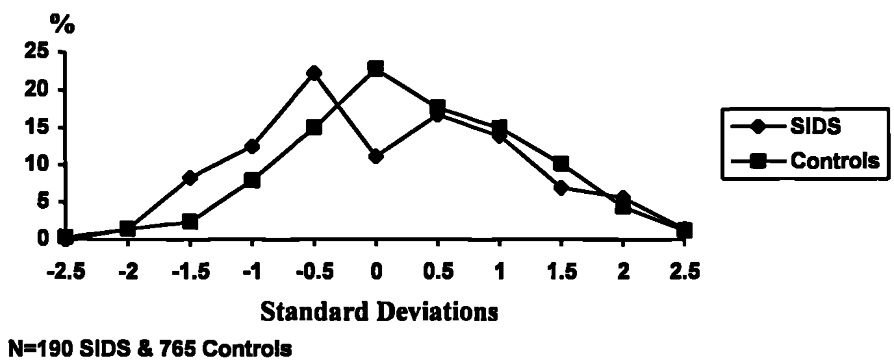


Figure 4.6 shows the results for those infants whose mother did not smoke during pregnancy. The two distributions were just significantly different (p=0.045).

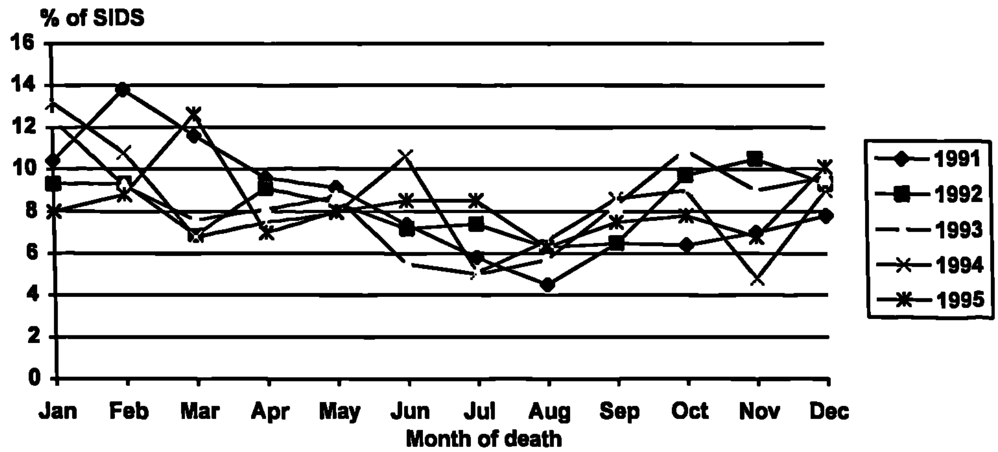
Taking into account the dose-response relationship of maternal smoking during pregnancy, and putting the birthweight z-scores into the same model, infant birthweight remained significant when mothers smoked 1 to 9 cigarettes a day (p=0.01) and when mothers smoked 10 to 19 cigarettes (p=0.01) but became non-significant when mothers smoked 20 or more cigarettes a day (p=0.06). Interpretation is limited because of small stratum-specific sample sizes but there appears to be weak evidence suggesting maternal smoking during pregnancy explains some of the low birthweights amongst the index infants in terms of a dose-response relationship. Low birthweight and maternal smoking during pregnancy may play an important role in the aetiology of SIDS but the interpretation is difficult as the strength of any findings may be compromised in the multivariable analysis because of the cause-effect relationship between them.

Features that have changed

Major epidemiological features to change since the reduction in incidence include a reduction in the previous high winter peaks of death and a shift of SIDS families to the more deprived social grouping. Unlike some previous studies, this study did not show that smaller infants died at a later age, a predominance of post-term births amongst the SIDS infants or greater episodes of sweating amongst multiparous infants.

We saw earlier in figure 1.3 the seasonal distribution of SIDS infants from 1985 to 1990 in England and Wales with the characteristic winter peak forming a u-shaped curve.

Figure 4.7 Seasonal distribution of SIDS infants in England & Wales 1991-95



Source : ONS health and population monitor [180]

Figure 4.7 plots the same data for the period 1991 to 1995. The distribution for this latter period, which covers the CESDI SUDI study, was much less pronounced, with slightly more deaths from January to March and slightly less in August. Given that the national data also includes deaths from unrecognised previous infections, which often occur in the winter months, the distribution of SIDS infants may be even less pronounced. The lack of seasonal pattern found in the CESDI SUDI study appears to be in line with the national trend and confirms similar findings by Ponsonby [132] in the latter years of the Tasmanian study. Previous studies found that the seasonal distribution was far more marked in infants aged over 12 weeks and an excess of male deaths in winter. However, in this study there was little difference between infants who died in the colder months (October to March) or the warmer months (April to September) with regards to age. There was however a difference in gender, but in the opposite direction, a predominance of male deaths in the warmer months (69.5% SIDS males) rather than the cooler ones (51% SIDS males), this difference was significant (OR=2.34 [95% CI :1.41 to 3.90]). A study by Buvé in the UK also suggested an increase of SIDS amongst the higher social classes in Winter. In this study, using receipt of Income Support as a marker for socio-economic status, fewer of the SIDS infants who died in the colder months were from families who received this income (28.0%) compared to those who died in the warmer months (40.4%) but this difference was not significant (p=0.11).

Some of the studies conducted before the fall in incidence suggested that infants with low birthweight, pre-term infants and those exposed to tobacco smoke died at an older age. These findings are not supported by this study. Infants of low birthweight (<2500g) actually had a lower median age (86.5 days [Interquartile range : 50 days to 139 days]) compared to those infants weighing greater than 2500g (92 days [Interquartile range : 62 days to 157 days]). Similarly, infants with a gestational age of 35 weeks or less had a lower median age (86 days [Interquartile range : 47 to 138 days]) compared to those infants with a higher gestation (91.5 days [Interquartile range : 47 to 138 days]). The median age of infants exposed to at least one hour of tobacco smoke a day (104.5 days [Interquartile range : 69 to 181 days]) was slightly higher than those who were not (101 days [Interquartile range : 65 to 162 days]) but this was not significant.

Some previous studies found a higher frequency of SIDS amongst the post-term infants, in this study approximately 5% of both SIDS and control infants were delivered after 41 weeks (OR=1.09 [95% CI : 0.50 to 2.33]).

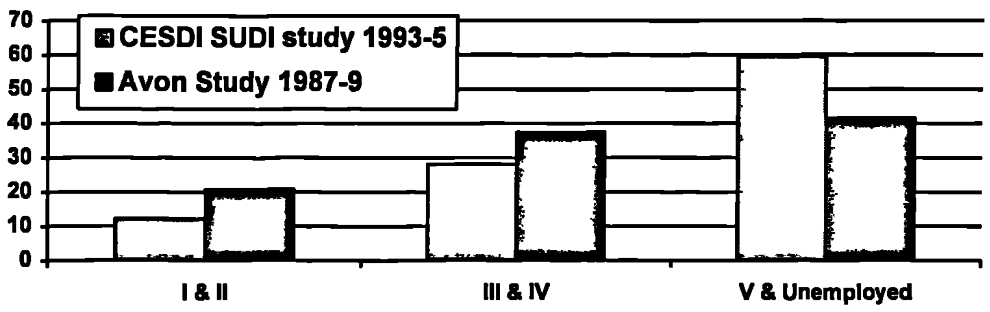
Of the 195 SIDS infants, 10 (5%) in this study were one of a pair of twins compared to 5 controls (0.6%). The numbers are too small for any meaningful comparison but do not support results found by Kahn in Belgium and France [82] specifically comparing 42 twins one of which had died of SIDS. Kahn found the SIDS twins to be significantly smaller with greater episodes of cyanosis or pallor and repeated episodes of profuse sweating during sleep. The median gestational age of the SIDS twins in this study was slightly higher than the control twin infants (36 weeks vs 35 weeks), whilst the birthweight centiles were half a standard deviation lower (-0.81 sd vs -0.27 sd). Of the 15 multiparous infants none were noted to be pale in the 24 hours before the death or reference sleep and only one was noted to be profusely sweating and this was a control infant.

A greater proportion of SIDS families in previous studies were consistently reported to have lower socio-economic status. Using the crude statistic of the unemployed or unskilled labourer as a proxy marker for socio-economic status, most studies reported a univariable odds ratio of just over 2. If we compare the unemployed (ignoring previous occupation) and unskilled labourers in this study with the semi-skilled, skilled and professional occupations, the degree of risk associated with the difference was much higher (OR=4.17 [95% CI : 2.92 to 5.95]) suggesting a further shift of SIDS families to lower socio-economic status. This statistic is dependent on the accuracy with which the control population in the study truly reflects the occupational classification of the whole population. Table 4.2 compares the occupational classification of control families in this study with data from the 1991 UK census of families with dependent children aged one and under.

Table 4.2 - Comparing occupational classification of study control families with families from the UK 1991 census		
Occupational Classification	UK 1991 census*	Study Controls
I	1.8%	1.4%
II	20.3%	21.3%
III	40.2%	38.5%
IV	15.9%	15.1%
V	3.5%	4.2%
Unemployed	18.3%	19.5%
* Families with dependent children aged one and under Data specially commissioned from the OPCS		

The study controls appear to closely represent the families from the whole population suggesting the findings regarding socio-economic status are reliable. The shift in socio-economic status is further demonstrated in Figure 4.8, comparing occupational classification amongst SIDS families in this study with an earlier study conducted in the county of Avon (part of this study's catchment area) before the fall in SIDS incidence.

Figure 4.8 - Shift in socio-economic status



The number of SIDS families in the poorest strata has risen from just over 40% to 60%.

Further information associated with low socio-economic status was gathered to try and uncover specific differences between SIDS and control families. The differences appeared across a broad spectrum. SIDS parents had less income and were more poorly educated, the housing conditions were in a worse state of repair, were more overcrowded and more SIDS parents lived in rented accommodation. We measured disruption in terms of moving house and type of accommodation such as bedsits and caravans and found a significantly higher proportion of SIDS families suffered more disruption. Fewer mothers were supported by a partner, and although there was no difference in the support forthcoming from family and friends nearly a half of all SIDS families were without a telephone or their own personal transport. The SIDS parents used more illegal drugs, mainly cannabis, drank more alcohol, and SIDS infants were exposed to more tobacco smoke. Although most of these factors are not easily modifiable in the same way as say the position in which the infant sleeps, the shift to lower socio-economic status will make it easier to identify high risk families from birth.

Identifying high risk families

Risk scoring systems have previously been attempted [70, 181-185] with little success. Some of these prediction schemes have been limited by inadequate diagnostic criteria, inadequate assignment procedures to weighted variables and using inappropriate populations such as the same population that has been used to develop the scoring system. Of those that were adequately designed and tested such as the Oxford and Sheffield SIDS risk prediction scores, a high sensitivity score (number of cases identified) was compromised by a specificity ([1 - specificity] is the proportion of population at high risk) not high enough to target a reasonably small proportion of the population or *vice-versa*. Both systems were tested over a five-year period in the Avon Area Health Authority [186] between 1983 and 1987, the Oxford system *identified 55%* of SIDS cases from 22% of the population whilst the Sheffield system *identified 35%* from 11% of the population. Results from this study suggest that a larger proportion of high risk families can be identified from a smaller proportion of the population.

The CESDI SUDI study reported in this thesis was extended for a further year and covered two additional regions, Northern and Wessex. In this third year, data was collected from 130 SIDS families and 520 controls. The risk prediction scores calculated from the first two years could therefore be tested on the third year population. Removing those records with missing values for the variables being tested yielded 118 SIDS cases (90.8%) and 485 controls (93.3%) where full data was available.

To construct a risk score factors identifiable at birth and significant in the multivariable analysis for the first two years were selected. For ease of interpretation, continuous variables were re-assigned to appropriate multi-categorical variables. These factors were modelled together and all variables that remained significant were included in the scoring system. These factors were assigned a weighted value. The weighting of the variables was calculated by using the Wald chi-square statistic [187], computed by dividing the estimated coefficient of interest by its standard error, which has an approximate normal distribution, and squaring the resultant value which was then rounded to the nearest whole number. Table 4.3 shows the breakdown of the CESDI SUDI 'at risk' scoring system.

Table 4.3 - CESDI SUDI 'at risk' scoring system

Variables	Category	Score
Maternal age :	*27 to 21yrs old*	9
	20 yrs or less	22
Number of children :	*2 or 3 children*	11
	4 or more	23
Family in receipt of income support	*Yes*	17
Maternal smoking during pregnancy	*Yes*	12
Infant a twin or triplet	*Yes*	12
Marital status at interview	*single*	4
Gestational age	*36 weeks or less*	6
Birthweight Z-score :	*< -1.5 standard deviations*	5
	between -1.5 and -1.01	3
	between -1 and -0.51	1
Infant taken to SCBU	*Yes*	4

Using this scoring system on the two year dataset an appropriate cut-off score was taken as 45 or greater. This system was then applied to the third year dataset and 52.5% of SIDS infants were identified from 11.8% of the population.

Although most of this information is available from hospital records and within the first week of the infant's life, the length of time to identify such families may take longer than expected if collecting neonatal records or having to contact the family to clarify certain factors. An alternative much simpler scoring system is shown in Table 4.4. This was derived by taking those variables with the highest score from the previous model and developing a system where the largest number of 'high-risk' families were identified from the smallest group of the population.

Table 4.4 - CESDI SUDI 'at risk' scoring system [simplified]		
Variables	Category	Score
Maternal age	*< 26 years old*	1
Number of children	*3 or more children*	1
Social class IV,V or unemployed	*IV, V or unemployed*	1
Maternal smoking during pregnancy	*Yes*	1

Here, no weighting is given to the factors and a 'high-risk' family is classified as any family who meets at least 3 of the 4 above conditions. Using this system on the third year dataset, 41.5% of SIDS families were identified from 7.8% of the total population. Peters & Golding [188] pointed out when comparing different scoring systems that an increasing number of components in a system does not necessarily improve prediction. The simplified system above seems to bear this out. The four factors above can easily be identified from hospital records during the early stage of pregnancy with no need for any type of calculation. Obviously the CESDI SUDI 'at risk' scoring system needs to be extensively tested on further populations and work needs to be done on what else the risk scores may predict in terms of morbidity as well as mortality. Initial analysis does suggest however, that a larger proportion of 'high-risk' SIDS families can be predicted from a smaller proportion of the population since the fall in SIDS rate. This may partly be due to the shift in SIDS families to the more deprived socio-economic status.

Chapter 15

Comparison of major risk factors pre and post 1991

Sleeping position

Findings related to the sleeping environment have recently been published [189, 190]. Studies throughout the 1980's consistently demonstrated an increased risk associated with SIDS for infants put down in the prone position. In 7 of the 12 previous studies, prone-sleeping was more prevalent in the **control** population compared to the supine position. In the Avon study [27] conducted in 1987, 53% of control mothers put their infant prone compared to 38% supine. Results from the CESDI SUDI study suggest the 'Back to Sleep' campaign conducted in 1991 has had an effect. Amongst the control infants 64% usually slept supine, 33% were usually put down on their side and only 3% were usually put down prone. The risk associated with the prone position remains highly significant in all multivariable models yet it is the least common position amongst SIDS infants (16%). The intervention campaign advising parents to avoid the prone position was very successful, but some families have clearly not taken up this message. Given that the more deprived sections of the population are the least affected by such campaigns one would expect the prevalence of prone-sleeping would be much higher in the more deprived SIDS families. A recent study in Victoria, Australia [191], showed different risks associated with sleeping position amongst different groups of the population. However, if we stratify the risk of prone-sleeping across the social boundaries the risk remains constant. Clearly the message regarding infant sleeping position needs to again be underlined. Furthermore, this message also needs to be changed.

Part of the advice in 1991 was to lay infants down on their side as a safer alternative to the prone position. Results from this study suggest this is not a safe alternative. Whether the infant's lower arm was extended to prevent rolling prone or not, side-sleeping was a significant univariable factor. The risk associated with rolling from side to prone in this study, was extremely significant (OR=21.69 [95% CI : 8.84 to 53.20]). Although the risk associated with side-sleeping in the multivariable models was not as strong as the prone position, the population attributable risk (the number of deaths that would be saved if the factor was eliminated) was actually higher for the side position (18.4%) compared to the prone position (14.2%) because of the extent to which the side position was adopted. Further studies need to be conducted to establish whether the side-sleeping position is indeed a risk factor, but it certainly should not be recommended as a safe alternative to sleeping supine.

Thermal stress and covering

The effect of heavy wrapping found in Fleming's [27] and Ponsonby's [132] studies appears to be less significant in this study. Like these previous studies, during the last sleep the SIDS infants were wrapped approximately 1 tog warmer and more SIDS infants slept in a room where the heating was on for the duration of the sleep. But these effects disappeared when account was taken of other, more significant factors. What appears to be emerging as a greater risk is the effect of loose covering. Although the use of duvets and loose covering became non-significant when account was taken of all significant factors, the proportion of SIDS infants found with covers over their head dominates all models. Only 1.7% of SIDS infants were put down at the bottom of the cot but 9.0% were found in this position suggesting perhaps that the infants had wriggled into this position. Of the 34 SIDS infants found with covers over their head, 19 (55.9%) moved down the bed during the last sleep. Since the rejection of "accidental mechanical suffocation" as insufficient nomenclature to define cot death and the more rigorous Beckwith definition, very few studies have investigated type of bed covering and how these covers are arranged. Because these deaths are unobserved one can only speculate as to whether head covering is part of a causal chain or a result of a struggle before death. However, advising parents to avoid duvets and tuck covers in firmly is an achievable aim and carries no identifiable danger to the infant. To this end, the *"Feet to Foot"* campaign has been launched in the UK by the Foundation into the Study of Infant Death, advising parents to place the feet of the infant at the foot of the cot, to avoid duvets and firmly tuck in the bedding.

Bed-sharing

Infants sharing the parental bed for the last/reference sleep was shown to be a significant univariable factor in 2 previous studies. In this study, Table 3.16 showed that bed-sharing for the whole night remained a significant factor after controlling for other variables. This was not because the infant slept between parents or because the infant was ill and brought into the bed; bed-sharing was the usual practice and most infants slept adjacent to one parent. Interpretation of these findings are difficult for several reasons. The usual practice of bed-sharing was not a significant risk factor in the temporal model confirming similar findings of previous studies by Lee [105] and Klonoff-Cohen [135-7]. In cultural groups in which bed-sharing is the norm, SIDS rates are consistently lower than in groups in which this is not the usual practice [192]. Studies of parental-baby interactions in sleeping laboratories have found that mothers who routinely bed-shared exhibited increased sensitivity to the presence of the baby in the bed than those who did not, and infants who routinely bed-shared showed more transient arousals, even when sleeping alone [193].

In this study there are certain factors such as recent maternal alcohol consumption that may partly explain the risk associated with bed-sharing. Other factors such as maternal smoking after pregnancy make it difficult to generalise the risk of bed-sharing to the whole population. The proportion of SIDS mothers who smoked after pregnancy (66.2%) was even higher amongst bed-sharing SIDS mothers (86.2%). The risk associated with bed-sharing amongst non-smoking mothers was not significant.

Breast-feeding

Many of the previous studies have found breast-feeding to have a protective effect in the univariable analysis. This study was no different. However, looking at the duration of breast-feeding, there seemed no clear dose-response effect. Breast-feeding was less protective up to 4 weeks compared to less than one week suggesting that it was acting as a marker of the lifestyle of mothers who breast-fed rather than showing a biological effect in itself. Table 3.16 also shows that the significance of breast-feeding quickly disappeared when other variables were added to the model, just adding maternal smoking for instance weakened breast-feeding to a non-significant finding (OR=0.78 [95% CI : 0.53 to 1.14]). This study does not lend weight to the evidence that breast-feeding is protective for SIDS but there are many other good reasons as to why this should be adopted as the best feeding practice.

Use of dummy

The apparent protective effect of a dummy is in agreement with Mitchell's recent study in New Zealand [122], the only other study to have looked at this factor. Although socio-economic status does not explain the possible protective effect associated with dummy use, this habit is more common in the more socio-economically deprived groups in the UK and is the only factor over-represented in these groups that is associated with a significantly reduced risk of the syndrome. Thus in the two models presented in Table 3.16, the protective effect is increased as further variables under-represented in the deprived group are added.

A report that dummy use has an adverse effect on breast-feeding [194] was supported by the findings of this study. Of those infants who often or always used a dummy more than a half did not breast-feed and less than a third breast-fed for more than 4 weeks. Of those infants who rarely used a dummy, two thirds breast-fed and nearly a half breast-fed for more than 4 weeks. The apparent univariable protective effect of breast-feeding, significant amongst infants who did not usually use a dummy (OR=0.48 [95% CI : 0.32 to 0.73]), was not significant amongst those who did (OR=0.63 [95% CI : 0.34 to 1.16]).

In both the univariable analysis and the multivariable models it appears that dummy use on the last night/ reference sleep had some sort of protective effect. Conversely, however, infants who usually have a dummy but had no dummy for the last/ reference sleep were more at risk. It could be hypothesised that dummy use plays a role in the respiratory pattern of the infant similar to thumb or finger sucking. If dummy use replaces the habit of thumb-sucking then dummy users could be at a disadvantage if a dummy was not provided or falls out during a sleep. This is purely speculative and requires an additional study, but demonstrates that the results could be interpreted in completely different ways.

Change in family routine

Significantly more of the SIDS families had a change in family routine in the 24 hours before the death of their infant. This variable remained significant in the temporal model, although it was one of the last set of factors to be added. However, this variable was also significant in the empirical model when all the risk factors were tested together. The description of the changes in routine are given in Table 2.75. Examining the 'changes' described, the level of importance attached to some of the changes in routine ascribed by the index parents appear higher than that ascribed by the control parents. This variable could be subject to recall bias. The acute memories of a grieving parent after the sudden loss of a child, painfully trying to recollect whether they could of done anything different, compared to asking control parents to recollect any change in routine from just another normal day is difficult to control for. Some of the reasons the SIDS parents gave reflect this; "Went to bed earlier than usual", "Baby had first bath", "let friend feed the baby". Although the factor measuring a change in family routine was significant, the actual change in routine appears quite insignificant.

Moving accommodation

In the univariable analysis, significantly more SIDS families moved accommodation once, before and after birth, compared to control families, and significantly more SIDS families moved accommodation more than once. However, in the empirical model, moving house once remained significant, but moving house more than once did not. In the temporal model, moving house before the birth remained significant but moving house after the infant was born did not. Only one SIDS family gave the reason " just moved to new accommodation" as a recent change in family routine. Under closer scrutiny, the factor measuring families moving to new accommodation appears to be more of a general disruptive marker for insecure tenure than acute disruption in terms of continually moving home or specifically moving home near to the time of the infant's death.

Health of the infant

More of the SIDS infants had a shorter gestation, were resuscitated at delivery using intubation or CPR and were admitted to SCBU. One of these factors remained in each multivariable model. SIDS infants were of lower birthweight regardless of gestation and sex and although some of this difference was explained by the excess of SIDS mothers smoking during pregnancy, birthweight remained in each multivariable model. SIDS infants also had more congenital and neonatal problems although no one problem was characteristic of SIDS and the difference did not remain significant when controlled for other factors. More of the SIDS infants were also prone to convulsions and fits and more of the SIDS infants had experienced at least one episode of lifelessness. This latter variable remained in every multivariable model. Recalling apparent life-threatening events may be subject to bias as SIDS parents may interpret minor episodes as something more important. However a similar proportion of SIDS and control infants had more than one episode and a similar proportion of parents called the GP and took their infant to hospital, suggesting this bias was limited. A significant proportion of SIDS infants were admitted to hospital for other reasons, although few of these reasons were life-threatening and this factor did not remain significant in the multivariable models. What did remain significant in the empirical model and just failed to achieve significance in the temporal model was the factor quantifying recent serious illness in the week before death. Nearly a quarter of the SIDS infants were unwell in the week before the death, of which more than half required medical attention (this compared to 10.6% of controls of which 5.3% required medical attention). If the "Cambridge Babycheck" was widely used, some of the SIDS infants would have been under medical observation before the point of death. Whether this would have altered the outcome can only be speculated.

The findings from this study suggest that not all SIDS infants were previously healthy and normal and that previous apparent life-threatening events should alert the health professionals to an elevated risk of SIDS.

Type of baby mattress

Media coverage has drawn much attention to the association of SIDS and fungal growth on PVC mattresses generating poisonous gases. Although this hypothesis has caused much concern to parents and to health professionals there is very little relevant published information. Proponents of this theory claim that old PVC mattresses, especially those used by other infants are the ones associated with the greatest risk. Results from this study do not support this hypothesis. There was no significant differences regarding the age and previous use of PVC mattresses which were widely used by both SIDS and control infants, significantly more so by the latter group.

Exposure to tobacco smoke

Findings concerning the risk associated with smoking have recently been published [195-198]. Maternal smoking during pregnancy was a significant finding in nearly every study that looked at this risk factor. In this study there was a strong dose-response effect in the univariable analysis, the risk increased with the more cigarettes the mother smoked. When controlled for several confounders, maternal smoking during pregnancy remained a significant factor. Smoking was more prevalent amongst mothers with low income, of lower social class and mothers who consumed greater quantities of alcohol, but the risk associated with smoking remained significant across the social divide.

In only 16.9% of index households did neither parent smoke, the population attributable risk for smoking by at least one parent was 61.2%. Paternal smoking remained a significant factor both in the temporal model and in the more specific model controlling for several possible confounders. Measuring daily postnatal exposure of tobacco smoke to the infant by parental estimation, showed a strong dose-response effect and remained a significant factor in all multivariable models. Clearly the risk to infants is not just from the mother during pregnancy but from all smokers.

In the absence of experimental evidence, regarded by many as a necessary and sufficient condition for identifying causal associations, epidemiologists have identified a number of criteria [199] that, taken together, would make it 'more provident to act on the basis that the association is causal rather than to await further evidence' [200]. These criteria are largely based on those set down by Bradford Hill in the 1960's [201], including strength and consistency of findings between studies, biological plausibility, coherence with other known facts and where applicable a temporal sequence and biological gradient. Certainly, the first two of these criteria have been fulfilled. The evidence from previous studies consistently support a strong association between SIDS and maternal smoking during pregnancy, evidence from this study after the fall in incidence, was as strong if not stronger. Many other studies have shown cigarette smoking in pregnancy retards fetal development; with regard to postnatal passive smoking, the suggestion of its possible causal role is coherent with the theories that ascribe SIDS to congenital respiratory abnormalities [202] or respiratory infections [203]. There could also be a direct link between smoking and SIDS if the risk were related to the action of a toxic agent in tobacco smoke such as carbon monoxide [204]. Clearly the risks associated with smoking and SIDS is biologically plausible. By coherence, Hill meant that the assumption of a causal relationship should not conflict with what is known about the disease. There does not appear to be such a conflict. The criterion for a temporal sequence has also been fulfilled as the risk factor precedes the event, in this case death. Finally a biological gradient which has clearly been demonstrated with the dose-response effect both during pregnancy and with postnatal exposure. It appears from the results of this and previous studies, we would be provident to act. Given the absence of experimental evidence, the association between infant exposure to tobacco smoke and SIDS is all but causal.

Chapter 16

Summary

The current epidemiology & risk factors of SIDS

The remarkable fall in the incidence of Sudden Infant Death Syndrome since the "Back to Sleep" campaign in 1991 has been accompanied by a striking reduction in the previously consistent winter peak of deaths. There remains an excess of deaths amongst boys but only in the warmer months between April and September. The previously recognised association between SIDS and socio-economic deprivation is now more marked than before the "Back to Sleep" campaign.

Many of the epidemiological features associated with SIDS found in previous studies have remained the same despite the fall in incidence. These include the same characteristic age distribution, low maternal age, single mothers, higher number of children, multiple births, lower birthweight and shorter gestation.

The adverse effects of the prone-sleeping position as a risk factor have been confirmed. A new finding is the possible risk associated with the side-sleeping position, previously recommended as a safer alternative to prone-sleeping. This factor was significant when looking at factors specifically associated with the sleeping and thermal environment, remained significant in the empirical model and just failed to reach significance when looking at variables over time . This added risk seems to result mainly from the tendency of babies placed on their sides to roll prone and was not influenced by the position of the infant's arm. The possible risk associated with side-sleeping needs to be confirmed but the higher prevalence of side-sleeping than prone-sleeping in the present population means that the population attributable risk from side sleeping (18.4%) is higher than that of prone sleeping (14.2%) despite a much lower odds ratio.

Interpretation of the effects of bed-sharing on the risk of death is complicated by the interactions with several other factors. Mothers who habitually take their babies into bed with them are not homogeneous but come from disparate ethnic, social, and cultural groups with very different approaches to child care, breast-feeding, smoking and alcohol misuse. The data confirms that bed-sharing is a risk factor amongst mothers who smoke.

This study has clearly shown exposure to tobacco smoke to be a strong risk factor. The responsibility of minimising the risk of the sudden infant death syndrome lies not just with the mother who smokes but all smokers. An appropriate public health message might be that smoking in the same environment as a pregnant mother or child is as unacceptable as drinking and driving. Parents who have been unable to give up or reduce their smoking habit should be strongly advised to keep their baby in a 'smoke-free zone'. This, however, should not be regarded as an alternative to the much better precaution of not smoking at all.

Certain factors, whilst they are apparently significant in the univariable analysis, are not found to be significant on multivariable analysis. Such factors include over-wrapping and breast-feeding.

An intriguing finding of the present study is the confirmation of the previous observation in the New Zealand study that there is an apparent effect from the use of a dummy. Whether the effect is protective or not depends on interpretation of the results. It will clearly be necessary to examine the interaction between dummy use and, for example, thumb-sucking and the effects on duration of breast-feeding before a recommendation can be given on the routine use of dummies.

Whilst the majority of SIDS infants appeared to be well in the week before the death, over a quarter were not and some of these infants required medical attention. Using a parental scoring system such as the "Cambridge Babycheck" may help detect infants at risk.

Families at risk, babies at risk and circumstances of risk

From the preliminary multivariable analysis of the results of this study, a picture has emerged of certain features of the family, the baby and the circumstances which are associated with increased risk of SIDS. Some of these features are potentially more amenable to change than others, whilst other features may serve as "markers" of the family, or infant, at risk and may be used by health care professionals to target appropriate health care and advice.

Factors for healthcare professionals to note

(i) Factors which are amenable to change by advice from health care professionals

e.g. infant sleeping position, heavy wrapping the use of duvets, loose bedding or head covering.

(ii) Factors which may be amenable to modification by advice from health care professionals, but which involve a change in parental behaviour

e.g. post-natal exposure to cigarette smoke or bed-sharing, particularly by parents who smoke or drink alcohol.

(iii) Factors which, whilst potentially amenable to change will require the development of a strategy to achieve a significant change in parental behaviour

e.g. parental smoking, parental alcohol or other drug abuse.

(iv) Factors which may alert health care professionals to the special needs of the family

e.g. low maternal age; high maternal parity ; low income; maternal smoking during pregnancy (three of these four factors identify over 40% of SIDS families); poor or crowded housing; single unsupported mother; baby of low birth weight; short gestation or multiple birth; and recent move of house (especially before the pregnancy).

(v) Acute factors which may signify transient increased risk and alert family or health care professionals to the need for close observation or possible treatment

e.g. a high "Baby-check" score or a history of an apparent life-threatening event.

The messages for parents which emerge from this study can be summarised as follows:

Whilst it is not possible to guarantee that an infant will not die as a cot death, by following certain simple guidelines the risk can be very substantially reduced:

1. Place your baby to sleep on his/her back, not the front or side.

2. Place your baby to sleep so that his/her feet are close to the foot of the cot ("feet

to foot") with the bedding securely tucked in and no higher than the baby's chin. Use blankets rather than a duvet. Check your baby to ensure that he/she does not become too hot or too cold.

3. Do not smoke during pregnancy or go in any room in which others are smoking.

4. Do not smoke in any room in which young infants ever go. Keep your baby out of rooms in which people smoke (i.e. maintain a "smoke-free zone" around yourself whilst pregnant, and around your baby).

5. If your baby is unwell, particularly if he/she has a temperature, has any difficulty breathing (e.g. showing signs of indrawing of the chest), or is less responsive than usual seek medical help promptly.

6. Whilst it is safe to take your baby into bed with you to feed or for comfort, it is preferable to place him/her back in the cot before you go to sleep if you are a smoker or if you have consumed any alcohol.

Conclusions

The present study confirms the significance of some previously noted risk factors for SIDS, improves our understanding of the nature and role of some other factors and potentially allows the identification within the population of mothers with babies at significantly increased risk. The recognition of such babies' increased risk may allow appropriate targeting of health care advice and support, to ensure that the messages reach and are acted upon by those at greatest risk. There is a need for prospective evaluation of the value of targeted ("risk related") interventions of this type.

References

1 PJ Fleming
The implementation of risk reduction for SIDS in the UK
Proceedings of the Royal College of Physicians of Edinburgh 1995; 25: 213-220.

2 JJ McKenna, E Thoman, T Anders, A Sadeh, V Schectman, S Glozbach
Infant-parent co-sleeping in evolutionary perspective : Implications for understanding infant sleep development and SIDS
Sleep 1993; 16: 263-282.

3 *Soranus' gynecolgy*
Translated with an introduction by Owsei Temkin
Baltimore : The John Hopkins Press, 1956.

4 JT McNeill, HM Gamer
Medieval handbooks of penance
New York: Columbia University Press 1938.

5 G Norvenius
Is SIDS a new phenomenon
In : *SIDS New Trends in the Nineties*, TO Rognum (ed)
Scandinavian University Press 1995, 11-14.

6 Royal Society
Philosophical transactions of the Royal Society of London 1732; 422: 256.

7 SR Limerick CBE
Sudden infant death in historical perspective
J Clin Pathol 1992; 45 (Supplement) : 3-6.

8 Anonymous
Medical jurisprudence: infants found dead in bed [Editorial]
Lancet 1855; 4:103.

9 J Golding, S Limerick, A Macfarlane
Sudden Infant Death, patterns puzzles and problems
Shepton Mallet, Open Books Publishing Ltd 1985: 6-9.

10 A Lee
On the thymus gland: its morbid affections and the diseases which arise from its abnormal enlargement
Am J Med Sci 1842; 3 : 135.

11 J Jessop
Sudden death and the thymus gland
BMJ 1905; 2: 1586.

12 WH Willcox
Infant mortality from 'overlaying'
BMJ 1904 (September 24): 1-7.

13 WH Davison
Accidental Infant Suffocation
BMJ 1945; 251-252.

14 J Werne, I Garrow
Sudden deaths of infants allegedly due to mechanical suffocation
Am J Public Health June 1947; 37: 675-687.

15 PV Woolley
Mechanical suffocation during infancy
J Pediatr 1945; 26: 572-575.

16 H Abramson
Accidental mechanical suffocation in infants
J Pediatr 1944; 25 : 404-413.

17 AM Barrett
In : *Sudden death in infancy*, D Gairdner (ed)
London: Churchill, 1954 : 301.

18 JB Beckwith
The sudden infant death syndrome
Curr Probl Paediatr 1973; 3: 1-36.

19 JL Emery
Is sudden infant death syndrome a diagnosis? Or is it just a diagnostic dustbin?
BMJ 1989; 299: 1240.

20 J Huber
Sudden infant death syndrome: the new clothes of the emperor
Eur J Pediatr 1993; 152: 93-94.

21 BR Mitchell
British historical statistics
Cambridge University Press 1988: 15.

22 S Beal, H Blundell
Sudden Infant Death Syndrome related to position in the cot
Med J Australia 1978; 2: 217-218.

23 KS Saturnus
Plotzicher Kindstod - eine Folge der Bauchlage?
In : *Festschrift Professor Leithoff. Kriminalstatistik*, Heidelberg 1985; 67-81.

24 DP Davies
Cot death in Hong Kong : a rare problem?
Lancet 1985; ii: 1346-9.

25 GA de Jonge, AC Engleberts, Koomen-Liefting, PJ Kostense
Cot death and prone sleeping position in the Netherlands
BMJ 1989; 298: 722.

26 EA Mitchell, R Scragg, AW Stewart, DMO Becroft, BJ Taylor et al
Results from the first year of the New Zealand cot death study
NZ Med J 1991: 71-76.

27 PJ Fleming, R Gilbert, Y Azaz, PJ Berry, PT Rudd, AW Stewart, E Hall
Interaction between bedding and sleeping position in the sudden infant death syndrome : a population based case-control study
BMJ 1990; 301: 85-89.

28 K Fitzgerald, Director of SIDS Australia
[Personal communication]

29 C Hiley
Babies' sleeping position
BMJ 1992; 305 : 115.

30 *The Nurse's Guide* : or the right method of bringing up young children
(1729) London by "an eminent physician"; 17 : 46-48.

31 D Greene
Asymmetry of the head and face in infants and in children
Am J Dis Child 1930; 41: 1317-1326.

32 New York State Department of Health
Mechanical suffocation: leading cause of accidental death in early infancy
Health News 1945; 22: 9.

33 Editorial
Prone or supine?
BMJ 1961; 1304.

34 AJG Spoelstra, S Srikasibhandra
Pressure-volume relationship of the lung and position in healthy neonates
Acta Paediat Scand 1973; 62: 176-180.

35 J Masterson, C Zucker, K Schultz
Prone and supine positioning effects on energy expenditure and behaviour of low birthweight neonates
Pediatrics 1987; 89: 689-692.

36 RJ Martin, N Herrell, D Rubin, A Fanaroff
Effect of supine and prone positions on arterial tension in the preterm infant
Pediatrics 1979; 63: 528-31.

37 V Yu
Effect of body positioning on gastric emptying in the neonate
Arch Dis Child 1975; 50 : 500-504.

38 FCM Schwartz, A Fenner, J Wolfsdrop
The influence of body position on pulmonary function in low birth babies
S Afr Med J 1975; 49: 79-81.

39 PJ Fleming, N Muller, MH Bryan, AC Bryan
The effects of abdominal loading on ribcage distortion in premature infants
Pediatrics 1979; 64: 425-428.

40 SM Beal
Sleeping position and SIDS: Past, present and future
SIDS : New Trends in the Nineties, Scandinavian University Press 1995, 147-151.

41 RJ Light, PV Smith
Accumulating evidence : Procedures for resolving contradictions among different research studies
Harvard Educational Review 1971; 41: 429-471.

42 LV Hedges, I Olkin
In: *Statistical methods for meta-analysis*
Academic Press 1985: 1-15.

43 GB Jackson
Methods for integrative reviews
Review of Educational Research 1980; 50: 438-460.

44 GV Glass
Primary, secondary and meta-analysis of research
Educational researcher 1976; 5: 351-379.

45 GV Glass, B McGraw, ML Smith
In : *Meta-analysis in social research*
Sage publications, Beverley Hills & London 1981: 11-21.

46 JL Fleiss, AJ Gross
Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: a critique
J Clin Epidemiol 1991; 44: 2: 127-139.

47 S Yusuf
Obtaining medically meaningful answers from an overview of randomised clinical trials
Stat Med 1987; 6: 281-286.

48 HJ Eysenck
An exercise in mega-silliness
Am Psychol 1978; 33: 517.

49 HS Sacks, J Berrier, D Reitman, VA Ancona-Berk, TC Chalmers
Meta-analysis of randomized controlled trials
N Engl J Med 1987; 316: 450-455.

50 M Jenicek
Meta-analysis in medicine: Where we are and where we want to go
J Clin Epidemiol 1989; 42: 35-44.

51 CL Meinert
Meta-analysis: Science or religion?
Contr Clin Trials 1989; 10: 257S-263S.

52 F Biering-Sorensen, T Jorgcnscn, J IIilden
Sudden infant death in Copenhagen 1956-1971
Acta Paediatr Scand 1978; 67: 129-137.

53 JF Kraus, S Greenland, M Bulteys
Risk factors for sudden infant death syndrome in the US collaborative perinatal project
Int J Epidemiol 1989; 18: 113-119.

54 RL Naeye, B Ladis, JS Drage
Sudden infant death syndrome : A prospective study
Am J Dis Child 1976; 130 : 1207-1212.

55 R Steele , JT Langworth
The relationship of antenatal and postnatal factors to sudden unexpected death in infancy
Canad Med Ass J 1966; 94 : 1165-1171.

56 CD Protestos, RG Carpenter, PM McWeeny, JL Emery
Obstetric and perinatal histories of children who died unexpectedly (cot death)
Archives Dis Child 1973; 48: 835-841.

57 RG Carpenter, JL Emery
Identification and follow-up of infants at risk of sudden death in infancy
Nature 1974; 250: 729.

58 P Froggatt, MA Lynas, G MacKenzie
Epidemiology of sudden unexpected death in infants ('cot death') in Northern Ireland
Brit J Prev Soc Med 1971; 25: 119-134.

59 P Froggatt
Epidemiological aspects of the Northern Ireland study
In : *Sudden infant death syndrome,* AB Bergman, JB Beckwith, GC Ray (eds).
University of Washington Press, Seattle1970: 32-46.

60 J Fedrick
Sudden unexpected death in infants in the Oxford Record Linkage area. The mother
British J Prev Soc Med 1974 ; 28: 93-97.

61 J Fedrick
Sudden unexpected death in infants in the Oxford Record Linkage area. An analysis with respect to time and space
British J Prev Soc Med 1973 ; 27: 217-224.

62 J Fedrick
Sudden unexpected death in infants in the Oxford Record Linkage area. Details of pregnancy, delivery and abnormality in the infant
British J Prev Soc Med 1974 ; 28: 164-171.

63 J Golding
More on oxytocin for induction of labor and sudden infant death syndrome
New Eng J Med 1986; 315: 192-193 (letter).

64 PJ Rintahaka, J Hirvonen
The epidemiology of sudden infant death syndrome in Finland in 1969-80
Forens Sci Int 1986; 30: 219-233.

65 GN Schrauzer, WJ Rhead, SL Saltzstein
Sudden infant death syndrome : Plasma vitamin E level and dietary factors
Ann Clin Lab Sci 1975; 5: 31-37.

66 AB Bergman, LA Wiesner
Relationship of passive cigarette-smoking to sudden infant death syndrome
Pediatrics 1976; 58: 665-668.

67 SL Tonkin
Infant mortality. Epidemiology of cot deaths in Auckland
NZ Med J 1986; 99: 324-326.

68 J Golding, S Limerick, A Macfarlane
Summary of the epidemiological findings
In : *Sudden infant death: Patterns puzzles and problems*
Shepton mallet Publishing Ltd, Open Books 1985: 104-136.

69 RG Carpenter, A Gardner, E Pursall, PM McWeeny
Identification of some infants at immediate risk of dying unexpectedly and justifying intensive study
Lancet, 1979: 343-346.

70 RG Carpenter, A Gardner, P Mcweeny, JL Emery
Multistage scoring system for identifying infants at risk of unexpected death
Arch Dis Child, 1977; 52 : 606-612.

71 JL Luke
Sleeping arrangements of sudden infant death syndrome victims in the District of Columbia - A preliminary report
J Forensic Sciences 1978: 379-383.

72 AG Getts, HF Hill
Sudden infant death syndrome: incidence at various altitudes
Develop Med Child Neurol 1982; 24: 61-68.

73 GM Buck, AM Michalek, AA Kramer, RE Batt
Labor and delivery events and risk of sudden infant death syndrome (SIDS)
Am J Epidemiol 1991; 133: 900-906.

74 GM Buck, DL Cookfair, AM Michalek, PC Nasca, SJ Standfast, LE Sever
Assessment of in utero hypoxia and risk of sudden infant death syndrome
Paed and Perinat Epidemiol 1989: 3: 157-173.

75 SJ Standfast, S Jereb, DT Janerich
The epidemiology of sudden infant death syndrome in upstate New York: birth characteristics
Am J Pub Health 1980; 70: 1061-1067.

76 AL Williams, EC Uren, L Bretherton
Respiratory viruses and sudden infant death syndrome
BMJ 1984; 288: 1491-1493.

77 J Knowelden, J Keeling, JP Nicholl
A multicentre study of post-neonatal mortality
London: *HM Stationary Office*: 1985.

78 JP Nicholl, A O'Cathain
Antenatal smoking, postnatal passive smoking and sudden infant death syndrome
In : *Effects of smoking on the fetus, neonate and child*, D Poswillo, E Alberman (eds)
Oxford: Oxford medical Publications, 1992.

79 AN Stanton, MAPS Downham, JR Oakley, JL Emery, J Knowelden
Terminal symptoms in children dying suddenly and unexpectedly at home
BMJ 1978: 1249-1251.

80 R Sunderland, JL Emery
Febrile convulsions and cot death
Lancet 1981: 176-178.

81 A Kahn, D Blum, P Hennart
A critical comparison of the history of sudden-death infants and infants hospitalised for near-miss for SIDS
Eur J Pediatr 1984; 143: 103-7.

82 A Kahn, D Blum, MF Muller, L Montauk, A Bochner, N Monod, P Plouin et al
Sudden infant death syndrome in a twin: A comparison of sibling histories
Pediatrics 1986; 78: 146-150.

83 HJ Hoffman, JC Hunter, NJ Ellish, DT Janerick, J Goldberg
Adverse reproductive factors and the sudden infant death syndrome
In: *Sudden infant death syndrome : Risk factors and basic mechanisms*, RM Harper, HJ Hoffman (eds)
New York: PMA Publishing Corp, 1988: 153-175.

84 HJ Hoffman. LS Hillman
Epidemiology of the sudden infant death syndrome: maternal, neonatal, and postneonatal risk factors
Clinics in perinatology 1992; 19: 717-737.

85 HJ Hoffman, JC Hunter, K Damus, J Pakter, DR Peterson, G van Belle, EG Hasselmeyer
Diphtheria-Tetanus-Pertussis immunization and sudden infant death: results of the national institute of child health and human development co-operative epidemiological study of sudden infant death syndrome risk factors
Pediatrics 1987; 79: 598-611.

86 M Wagner, D Samson-Dollfus, J Menard
Sudden unexpected infant death in a French county
Arch Dis Child 1984; 59: 1082-1087.

87 TG Matthews, S O'Brien
Sudden infant death syndrome in an Irish population
Irish Med J 1985; 78: 251-253.

88 VA Stebbens, JR Alexander, DP Southall
Pre- and perinatal clinical characteristics of infants who suffer sudden infant death syndrome
Biol Neonate 1987; 51: 129-137.

89 EM Taylor, JL Emery
Immunisation and cot death
Lancet 1982; 721 [Letter].

90 EM Taylor, JL Emery
Family and community factors associated with infant deaths that might be preventable
BMJ 1983; 287: 871-874.

91 EAS Nelson (MD Thesis)
Sudden infant death syndrome and child care practices
Pub : EAS Nelson, University of Otago, Hong Kong 1996.

92 EAS Nelson, SM Williams, BJ Taylor, B Morris, RPK Ford
Postneonatal mortality in south New Zealand: necropsy data review
Paediatr Perinat Epidemiol 1989; 3 : 375-385.

93 MH Cameron, AL Williams
Development and testing of scoring systems for predicting infants with high-risk of sudden infant death syndrome in Melbourne
Aust Paediatr J (Suppl) 1986 : 37-45.

94 ND McGlashan
Sudden deaths in Tasmania, 1980-1986: A seven year prospective study
Soc Sci Med 1989; 29: 1015-26.

95 LM Alessandri, AW Read, FJ Stanley, PR Burton, VP Dawes
Sudden infant death syndrome in Aboriginal and non-Aboriginal infants
J Paediatr Child Health 1994; 30, 234-241.

96 LM Alessandri, AW Read, FJ Stanley, PR Burton, VP Dawes
Sudden infant death syndrome and infant mortality in Aboriginal and non-Aboriginal infants
J Paediatr Child Health 1994; 30, 242-247.

97 C Einspieler, J Widder, A Holzer, T Kenner
The predictive value of behavioural risk factors for sudden infant death
Early Hum Dev 1988; 18: 101-109.

98 A McLoughlin
Sudden infant deaths in Tameside
Health Visitor 1988; 61: 235-237.

99 H Wierenga, R Brand, T Geudeke, HP van Geijn, H van der Harten, SP Verloove-Vanhorick
Prenatal risk factors for cot death in very preterm and small for gestational age infants
Early Hum Dev 1990; 23: 15-26.

100 MR Karagas, KA Hollenbach, DE Hickock, JR Daling
Induction of labor and risk of sudden infant death syndrome
Obstet Gynecol 1993; 81: 497-501.

101 D-K Li, JR Daling
Maternal smoking, low birth weight, and ethnicity in relation to sudden infant death syndrome
Am J Epidemiol 1991; 134: 958-964.

102 S Beal, C Porter
Sudden infant death syndrome related to climate
Acta Paediatr Scand 1991; 80: 278-287.

103 A Buvé, LC Rodrigues
Sudden infant death syndrome: does winter affect poor and rich babies equally?
J Epidemiol Community Health 1992; 46: 485-488.

104 A Flahaut, A Messiah, E Jougla, E Bouvet, J Perin, F Hatton
Sudden infant death syndrome and diptheria/tetanus toxoid/pertussis/poliomyelitis immunisation
Lancet 1988: 582-583 (Letter).

105 NNY Lee, YF Chan, DP Davis, E Lau, DCP Yip
Sudden infant death syndrome in Hong Kong: Confirmation of a low incidence
BMJ 1989; 298: 721-722.

106 EAS Nelson, BJ Taylor, IL Weatherall
Sleeping position and infant bedding may predispose to hyperthermia and the sudden infant death syndrome
Lancet 1989, January 28: 199-201.

107 SM Williams, BJ Taylor, RPK Ford, EAS Nelson
Growth velocity before sudden infant death
Arch Dis Child 1990; 65: 1315-1318.

108 RPK Ford, HE McCormick, EAS Nelson, BJ Taylor
Plunket contacts in the first year of life
NZ Med J 1990; 103: 316-318.

109 IA Kelmanson
An assessment of the microsocial environment of children diagnosed as 'sudden infant death' using the 'process' inventory
Eur J Pediatr 1993; 58: 295-300.

110 S Bartholomew, BA MacArthur
Comparison of infants dying from the sudden infant death syndrome with matched live controls
Soc Sci Med 1988; 27: 393-397.

111 RE Gilbert, PJ Fleming, Y Azaz, P Rudd
Signs of illness preceding sudden unexpected death in infants
BMJ 1990; 300: 1237-1239.

112 R Wigfield, PJ Fleming
The prevalence of risk factors for SIDS: Impact of an intervention campaign
In : *SIDS New trends in the nineties*, TO Rognum (ed)
Scandanvian University Press 1995: 124-128.

113 R Gilbert, P Rudd, PJ Berry, PJ Fleming, E Hall, DG White, VOC Oreffo, P James, JA Evans
Combined effect of infection and heavy wrapping on the risk of sudden unexpected infant death
Arch Dis Child 1992; 67: 171-177.

114 EA Mitchell, BJ Taylor, RPK Ford, AW Stewart, DMO Becroft, JMD Thompson et al
Four modifiable and other major risk factors for cot death: The New Zealand study
J Paediatr Child Health 1992; 28(suppl): S3-S8.

115 EA Mitchell, RPK Ford, BJ Taylor, AW Stewart et al
Further evidence supporting a causal relationship between prone sleeping position and SIDS
J Paediatr Child Health 1992; 28 (Suppl): S9-S12.

116 EA Mitchell
Sleeping position of infants and the sudden infant death syndrome
Acta Paediatrica Suppl; 389: 26-30.

117 RKR Scragg, EA Mitchell, AW Stewart, RPK Ford, BJ Taylor, IB Hassall et al
Infant room-sharing and prone sleep position in sudden infant death syndrome
Lancet 1996; 347: 7-12.

118 EA Mitchell, JMD Thompson
Co-sleeping increases the risk of SIDS, but sleeping in the parents' bedroom lowers it
In : *SIDS New trends in the nineties*, TO Rognum (ed)
Scandanavian University Press 1995: 266-269.

119 R Scragg, EA Mitchell, BJ Taylor, AW Stewart, RPK Ford, JMD Thompson et al
Bed sharing, smoking, and alcohol in the sudden infant death syndrome
BMJ 1993; 307: 1312-1318.

120 EA Mitchell, RPK Ford, AW Stewart, BJ Taylor, DMO Becroft, JMD Thompson et al
Smoking and the sudden infant death syndrome
Pediatrics 1993; 91: 5: 893-896.

121 RPK Ford, BJ Taylor, EA Mitchell, SA Enright, AW Stewart, DMO Becroft, R Scragg et al
Breastfeeding and the risk of sudden infant death syndrome
Int J Epiemiol 1993; 22: 5: 885-889.

122 EA Mitchell, BJ Taylor, RPK Ford, AW Stewart, BMO Becroft et al
Dummies and the sudden infant death syndrome
Arch Dis Child 1993; 68: 501-504.

123 RPK Ford RPK, EA Mitchell, BJ Taylor
Well health care and the sudden infant death syndrome
J Paediatr Child Health 1994; 30: 140-143.

124 RPK Ford, EA Mitchell, R Scragg, AW Stewart, BJ Taylor, EM Allen
Factors adversely associated with breastfeeding in New Zealand
J Paediatr Child Health 1994; 30: 483-489.

125 CA Wilson, BJ Taylor, RM Laing, SM Williams, EA Mitchell
Clothing and bedding and its relevance to sudden infant death syndrome: further results from the New Zealand Cot Death Study
J Paediatr Child Health 1994; 30: 506-512.

126 R Scragg, AW Stewart, EA Mitchell, RPK Ford, JMD Thompson
Public health policy on bed sharing and smoking in the sudden infant death syndrome
NZ Med J 1995; 108: 218-222.

127 EA Mitchell, AW Stewart, M Clements, RPK Ford
Immunisation and the sudden infant death syndrome
Arch Dis Child 1995; 73: 498-501.

128 SM Williams, BJ Taylor, EA Mitchell
Sudden infant death syndrome: insulation from bedding and clothing and its effect modifiers
Int J Epidemiol 1996; 25: 366-375.

129 RPK Ford, PJ Schulter, BJ Taylor, EA Mitchell
Allergy and the risk of sudden infant death syndrome
Clin Experimental Allergy 1996; 26: 580-584.

130 S Gormally, TG Matthews
Contemporary risk factors for SIDS in Irish infants, a case control study
Irish J Med Sci 1992; 161: 23-24.

131 KC Schoendorf, JL Kiely
Relationship of sudden infant death syndrome to maternal smoking during and after pregnancy
Pediatrics 1992; 90: 905-908.

132 A-L Ponsonby, T Dwyer, LE Gibbons, JA Cochrane, ME Jones, MJ McCall
Thermal environment and sudden infant death syndrome: case-control study
BMJ 1992; 304: 277-282.

133 A-L Ponsonby, T Dwyer, LE Gibbons, JA Cochrane, Y-G Wang
Factors potentiating the risk of sudden infant death syndrome associated with the prone position
N Eng J Med 1993; 329: 377-381.

134 A-L Ponsonby, T Dwyer, SV Kasl, JA Cochrane
The Tasmanian SIDS case-control study: univariable and multivariable risk factor analysis
Paed & Peri Epidemiol 1995; 9: 256-272.

135 HS Klonoff-Cohen, SL Edelstein, ES Lefkowitz, IP Srinivasan, D Kaegi, JC Chang, KJ Wiley
The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrome
JAMA 1995; 273: 10: 795-798.

136 HS Klonoff-Cohen, SL Edelstein
Bed sharing and the sudden infant death syndrome
BMJ 1995; 311: 1269-1272.

137 HS Klonnoff-Cohen, SL Edelstein
A case-control study of routine and death scene sleep position and sudden infant death syndrome in Southern California
JAMA 1995; 273: 790-794.

138 RE Wigfield, PJ Fleming, PJ Berry, PT Rudd, J Golding
Can the fall in Avon's sudden infant death rate be explained by changes in sleeping position
BMJ 1992; 304: 282-283.

139 RE Gilbert, RE Wigfield, PJ Fleming, PJ Berry, PT Rudd
Bottle feeding and the sudden infant death syndrome
BMJ 1995; 310: 88-90.

140 EA Mitchell, L Scragg, M Clements
Factors related to infants bedsharing
NZ Med J 1994; 107: 466-467 (letter).

141 EA Mitchell, L Scragg , M Clements
Location of smoking and the sudden infant death syndrome (SIDS)
Aust NZ J Med 1995; 25: 155-156.

142 EA Mitchell, L Scragg, M Clements
Soft cot mattresses and the sudden infant death syndrome
NZ Med J 1996; 109: 206-207.

143 EA Mitchell, L Scragg, M Clements
Marital status and births after losing a baby from the sudden infant death syndrome
Eur J Pediatr 1996; 155: 712-716.

144 N Lewak, DJ van den Berg, JB Beckwith
Sudden infant death syndrome risk factors: Prospective data review
Clin Pediatr 1979; 18: 404-411.

145 AB Bergman
Sudden infant death syndrome in King County Washington: epidemiological aspects
In : *Sudden infant death syndrome*, AB Bergman, JB Beckwith, GC Ray (eds)
University of Washington Press, Seattle1970.

146 J Murphy, R Newcombe, J Sibert
The epidemiology of sudden infant death syndrome
J Epidemiol Community Health 1982; 36: 17-21.

147 LM Irgens, R Skjærven
Sudden infant death syndrome and post perinatal mortality in Norwegian birth cohorts 1967-1980
Acta Paediatr Scand 1986; 75: 523-529.

148 N. Øyen, R Skjærven, RE Little, AJ Wilcox
Fetal growth retardation in Sudden Infant Death Syndrome (SIDS) babies and their siblings
Am J Epidemiol 1995; 142: 84-90.

149 JF Kraus, NO Borhani
Post-neonatal sudden unexplained death in California: A cohort study
Am J Epidemiol 1972: 95: 497-510.

150 NM Newman
Sudden infant death syndrome in Tasmania 1975-81
Aust Paediatr J 1986; Suppl: 17-19.

151 A-L Ponsonby, T Dwyer, ME Jones
Sudden infant death syndrome: seasonality and a biophasic model of pathogenesis
J Epidemiol & Comm Health 1992; 46: 33-37.

152 SEM Bartholomew, BA Macarthur, AD Bain
Sudden infant death syndrome in south east Scotland
Arch Dis Child 1987; 62: 951-956.

153 M VandenBerg
Smoking during pregnancy and post-neonatal death
NZ Med J 1985; 98: 1075-1078.

154 MM Adams, PH Rhodes, BJ McCarthy
Are race and length of gestation related to age at death in the sudden infant death syndrome
Paed & Perinatal Epidemiol 1990; 4 : 325-339.

155 MH Malloy, JC Kleinman, GH Land, WF Schramm
The association of maternal smoking with age and the cause of infant death
Am J Epidemiol 1988; 128: 46-55.

156 MH Bouvier-Colle, J Inizan, E Michel
Postneonatal mortality, sudden infant death syndrome: factors preventing the decline of infant mortality in France from 1979 to 1985.
Paed & Perinatal Epidem 1989; 3: 256-267.

157 B Borman, J Fraser, G de Boer
A national study of sudden infant death syndrome in New Zealand
NZ Med J 1988; 101: 413-5.

158 S Tonkin, I Hassall
Infant sleeping position and cot death (letter)
Aust Paediatr J 1989; 25: 376-377.

159 B Haglund, S Cnattingius
Cigarette smoking as a risk factor for sudden infant death syndrome: A population-based study
Am J Public Health 1990; 80: 29-32.

160 H Bauchner, B Zuckerman, M Mcclain, D Frank, LE Fried, H Kayne
Risk of sudden infant death syndrome among infants with in utero exposure to cocaine
J Pediatr 1988; 113: 831-834.

161 KL Irwin, S Mannino, J Daling
Sudden infant death syndrome in Washington State: Why are native american infants at greater risk than white infants
J Pediatr 1992; 121: 242-7.

162 M Kilkenny, J Lumley
Ethnic differences in the incidence of the sudden infant death syndrome (SIDS) in Victoria, Australia 1985-1989
Paed Perinat Epidemiol 1994; 8: 27-40.

163 DJ Durand, AM Espinoza, BG Nickerson
Association between prenatal cocaine exposure and sudden infant death syndrome
J Peditrics 1990; 117: 909-911.

164 T Dwyer, AL Ponsonby, NM Newman, LE Gibbons
Prospective cohort study of prone sleeping position and sudden infant death syndrome
Lancet 1991; 337: 1244-1247.

165 T Dwyer, A-L Ponsonby, L Blizzard, N Newman, JA Cochrane
The contribution of changes in the prevalence of prone sleeping position to the decline in sudden infant death syndrome in Tasmania
JAMA 1995; 273: 783-789.

166 T Fujita, N Kato
Risk factors for SIDS in Japan: A record-linkage study based on vital statistics
Acta Paed Japonica 1994; 36: 325-328.

167 *OPCS Monitor*
Sudden infant deaths 1985-87
Crown Copyright; DH3 88/3: 3-5.

168 *OPCS Monitor*
Sudden infant deaths 1988-92
Crown Copyright; DH3 93/2: 4-5.

169 *SPSS Inc*
444 N Michigan Avenue, Chicago, Illinois 60611.

170 PS Blair, PJ Fleming, D Bensley, I Smith, C Bacon, E Taylor
Plastic mattresses and sudden infant death syndrome
Lancet 1995; 345: 8951: 720.

171 *SAS Institute Inc.*
SAS Campus Drive, Cary, North Carolina, USA.

172 P Bruzzi, SB Green, DP Byar, LA Brunton, C Schaiver
Estimating the population attributable risk for multiple risk factors using case control data
Am J Epidemiol 1985; 122: 904-914.

173 S Siegel
Nonparametric statistics
McGraw-Hill 1956 : 47-52.

174 *Fox-Pro*
Microsft Corporation, One Microsoft Way, Redmond, Washington, USA.

175 *National Statistics Monitor population and health*
Mid-1995 population estimates for England & Wales
Crown Copyright 1996; PP1 96/2: ONS Government statistical service: 10-16.

176 A Bridgewood, D Savage
General Household Survey 1991
Crown copyright 1993 OPCS; GHS (22): 9-12.

177 *Registrar General's 'Standard Occupational Classification'*
(developed by the Employment Department Group in collaboration with the OPCS)
HMSO Feb1990; Volumes I, II & III.

178 CJ Morley et al
Cambridge Babycheck
Arch Dis Child 1991; 66: 100-50.

179 GA de Jonge, Burgmeijer, AC Engelberts, J Hoogenboezem , PJ Kostense, AK Sprij
Sleeping position for infants and cot death in the Netherlands 1985-91
Arch Dis Child 1993; 69: 660-3.

180 *National Statistics Monitor population and health*
Sudden infant deaths 1991-95
Crown Copyright; DH3 96/2: 4.

181 EM Taylor, NJ Spencer, RG Carpenter
Evaluation of attempted prevention of unexpected infant death in very high-risk infants by planned health care
Acta Paediatr 1993; 82: 83-86.

182 JR Oakley, CJ Tavare, AN Stanton
Evaluation of the Sheffield system for identifying children at risk from unexpected death in infancy
Arch Dis Child 1978; 53: 649-652.

183 RG Carpenter, A Gardner, M Jepson, EM Taylor et al
Prevention of unexpected infant death
Lancet 1983; 39 : 723- 727.

184 ET d'Espaignet, T Dwyer, NM Newman, A-L Ponsonby, SG Candy
The development of a model for predicting infants at high risk of sudden infant death syndrome in Tasmania
Paed & Perinatal Epid 1990; 4: 422-435.

185 N Øyen, R Skjærven, LM Irgens
Population-based recurrence risk of sudden infant death syndrome compared with other infant and fetal deaths
Am J Epidemiol 1996; 144: 300-305.

186 JG Brooks, PJ Fleming, PJ Berry, J Golding
Evaluation of the Oxford and Sheffield SIDS risk prediction scores
Pediatric Pulmonology 1992; 14: 171-179.

187 DG Kleinbaum
In : *Logistic regression a self-learning text*
Statistics in the Health Sciences series, Pub Springer-Verlag New York 1994 : 134-135.

188 TJ Peters, J Golding
Prediction of sudden infant death syndrome: an independent evaluation of four scoring methods
Statistics in Medicine 1986; 5: 113-126.

189 PJ Fleming, PS Blair, C Bacon, D Bensley, I Smith, E Taylor, J Golding, J Berry, J Tripp
Environment of infants during sleep and risk of sudden infant death syndrome : results of 1993-5 case-control study for confidential inquiry into stillbirths and deaths in infancy
BMJ 1996; 313: 191-195.

190 PS Blair, IJ Smith, PJ Fleming, M Ward-Platt, D Hall, CJ Bacon, D Bensley et al
The CESDI SUDI study: Sleeping position, bedsharing and the sleeping environment in SIDS families
Anales Espanoles de Paed 1997; Supp 92: 24.

191 A Potter, J Lumley, L Watson
The 'new' risk factors for SIDS: is there an association with the ethnic and place of birth differences in Victoria, Australia?
Early Human Develop 1996; 45: 119-131.

192 EA Mitchell
Co-sleeping and sudden infant death syndrome
Lancet 1996; 348: 1466.

193 J Mckenna, S Mosko, C Richard
Infant arousals during mother-infant bedsharing: implications for infant sleep and SIDS research
Pediatrics 1997 (In press).

194 FC Barros, CG Victora, TC Semer, ST Filho, E Tamosi, E Weiderpass
Use of pacifiers is associated with decreased breastfeeding duration
Paediatrics 1995; 95: 497-499.

195 PS Blair, PJ Fleming, D Bensley, C Bacon, I Smith, E Taylor, J Golding, J Berry, J Tripp
Smoking and the sudden infant death syndrome : results of 1993-5 case-control study for confidential inquiry into stillbirths and deaths in infancy
BMJ 1996; 313: 195-198.

196 PS Blair, D Bensley, PJ Fleming, C Bacon, I Smith, E Taylor, J Tripp et al.
Smoking, cot mattress covers and other risk factors of sids : descriptive analysis after one year
European Journal of Pediatrics; Suppl : 154 : 5 : S5.

197 PS Blair, PJ Fleming, D Bensley, I Smith, C Bacon, PJ Berry.
Risk factors for SIDS after a national intervention campaign : The importance of parental smoking
Pediatric Pulmonology 1995; 20 : 5 : 335.

198 IJ Smith, PS Blair, PJ Fleming, M Ward-Platt, D Hall, CJ Bacon, D Bensley et al
The CESDI SUDI study: The shift to lower socio-economic status and the risk of infant exposure to tobacco smoke associated with SIDS
Anales Espanoles de Paed 1997; Supp 92: 28

199 MJ Elwood
Causal relationships in medicine. A practical system for critical appraisal
Oxford University Press 1988.

200 B McMahon, T Pugh
Epidemiology, principles and methods
Brown & Co, Boston 1970.

201 AB Hill
The environment and disease: Association or causation?
Proc Roy Soc Med 1965; 58: 295-300.

202 JV Wiel
Familial factors, ventilatory control, and sudden infant death
N Eng J Med 1980; 302: 517-519.

203 RA Franciosi
Respiratory infections as a trigger for Sudden Infant Death Syndrome
Minnesota Medicine 1985: 271-272.

204 CG Watkins, GL Strope
Chronic carbon monoxide poisoning as a major constituting factor in the sudden infant death syndrome
Am J Dis Child 1986; 140: 619.

205 EA Mitchell
Smoking: The next major and modifiable risk factor
In: *SIDS, New trends in the nineties,* TO Rognum (ed)
Scandanavian University Press 1995: 114-118.

206 N Lewak et al
Sudden infant death syndrome risk factors, prospective data review
Clin Paed 1979: 406-411.

207 AAM Gibson
Current epidemiology of SIDS
J Clin Pathol 1992; 45: 7-10 (Supplement).

208 RW Byard
Possible mechanism responsible for the sudden infant death syndrome
J Paediatr Child Health 1991; 27: 147-157.

209 S Beal, CF Finch
An overview of retrospective case-control studies investigating the relationship between prone sleeping position and SIDS
J Paediatr Child Health 1991; 27: 334-339.

210 RG Carpenter
Sudden and unexpected deaths in infancy (cot death)
In: *Sudden and unexpected deaths in infancy (cot death),* FE Camps, RG Carpenter, (eds)
Pub J Wright, Bristol 1972; 7-15.

211 SM Beal
Sudden infant death syndrome
MD Thesis, Flinde University of South Australia, Adelaide 1986.

212 A Engelberts
Cot death in the Netherlands : An epidemiological study
MD Thesis, Amsterdam: VU University Press 1991.

213 K-S Saternus
Plotzlicher kindstod : eine folge der bauchlage?
In : Prof L Festschrift. Heidelberg, Germany : *Kriminalistik Verlag* 1985: 67-81.

214 J Senecal, M Roussey, G Defawe, M Delhaye, B Piquemal
Procubitus et mort subite inattendue du nourrisson
Arch Fr Pediatr 1987; 44: 131-136.

215 ST Nilsen, A Laerdal
Krybbedød og røyking I svangerskapet
Tidsskr Nor Laegeforen 1991; 111: 3493-3495.

216 M-H Bouvier-Colle, V Varnoux, E Hausherr
Revue bibliographique des etudes sur la mort subiteen relation avec la position de sommeil chez le nourrisson
Proceedings of Reunion du Groupe d'Etudes de Langue Francaise sur la mort subite du nourrisson, Nice France 1990.

Appendix I

Search for previous SIDS studies

A comprehensive search for epidemiological SIDS studies from 1955 to 1996, case-control or cohort, was undertaken. The search is still ongoing and for the most part reproducible, outlined in the following steps

i) Titles of papers and many of the abstracts of major medical journals are listed in the Index Medicus. A computerised version is available in most medical libraries using MEDLINE. A search was conducted from 1966 to 1996 using the keywords 'SIDS', 'Sudden Infant Death Syndrome', 'Cot death' and 'Crib death'. Over 500 references were found of which over 50 were relevant papers reporting the results of SIDS studies.

ii) Utilising the efforts of previous searches,
  a) a further 10 papers were found from collections kept at University of Bristol.
  b) a further 20 papers (from 300 references) were found using the Australian SIDS database.
  (Contact addresses below)*

iii) From the above searches, several review articles were obtained [205-209] providing a handful of further papers.

iv) Networking with fellow researchers via e-mail has revealed 3 further studies. The intention is to publicise this search at forthcoming conferences, make the results freely available, and encourage collaboration to provide a definitive list of all the previous work in this field.

So far, the search has produced 51 case-control, 23 cohort and 3 case-series studies. Results of one study from 1958 [210] were unavailable because the book was out of print, 2 further studies were written up in PHD theses [211, 212] that are also as yet unavailable and 4 papers obtained required translation [213-216].

There were 3 unpublished studies found, two small case-control studies in London & Newcastle (Dr Chris Bacon, now retired) and one in Austria (C Einspeiler), neither author of which have any data available. There were also studies recently completed in Eire, Scandanavia, Germany and the USA that have not yet been published.

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Appendix II

Other factors reported by previous studies

Table A1 - Factors prior to or relating to pregnancy		
Risk Factor	Study Number	
	Significant	Non-Significant
Age of partner	*13, 27, 29, 49, 69*	*8, 23, 39, 42, 53*
Alcohol consumption (mother)	*29*	*21, 52*
Alcohol consumption (partner)		*21, 52*
Anemia	*3, 8, 24, 27*	*5, 52*
Bleeding during pregnancy	*5, 16, 30*	*7*
Blood levels abnormal	*27*	*2*
Coffee consumption	*19*	
Complications (including eclampsia)	*5, 7, 16, 24, 26, 30, 54, 73*	*21, 22, 60*
Consanguity		*3*
Contraceptives, Type used		*19*
Date of registration to clinic	*2, 54, 44, 57, 69, 73*	*60*
Fetal growth	*21*	
Fetal movements	*31*	
Height of mother	*12*	*3, 23, 30*
Hospital (type)	*30*	
Hospitalisation		*2, 5, 19*
Hydramnios		*2, 3*
Illegal drug use (mother)	*3, 21, 71, 73*	*68*
Illness/ Infection/ trauma	*5, 7, 12, 16, 21*	*13, 34*
LMP known	*30*	
Medication during pregnancy	*8*	*9, 21*
Planned pregnancy		*23, 52*
Prenatal visits/ classes	*2, 3, 4, 8, 15, 16, 21, 26, 27, 34, 35, 44, 52, 54, 57, 69*	*5, 19, 23, 49*
Previous abortion/requested	*2, 24, 69*	*3, 5, 7, 8, 21*
Previous congenital disorder(mother)		*3*
Previous deaths (infants)	*13, 21, 42*	*8, 23, 52*
Previous deaths (older children)	*5*	*3, 23*
Previous fetal deaths	*4*	*2, 3,6, 7, 21, 29, 52*
Previous pre-term births	*2*	*3, 23*
Previous problems during pregnancy	*29*	
Previous stillbirths	*21*	*2, 8, 74*
Proteinuria	*2, 3, 26*	*5*
Puerperal infection	*8*	
Time between pregnancies	*7, 13, 16, 21, 24, 51, 52, 60*	*12, 32, 45*
Toxemia		*3, 34*
Ultrasound scan/ X-rays	*21*	*3, 6, 21*
Vaginal/ Urinary infection	*3, 5, 13, 21, 26, 30, 43*	*12*
Weight gain during pregnancy	*21*	*2, 3*
Weight gain pre-pregnancy		*3*

Table A2 - Factors relating to labour and delivery		
Risk Factor	Study Number	
	Significant	Non-Significant
Anaesthesia used	*5, 13*	*16, 52, 23*
Augmented birth		*34*
Bag & Mask/Oxygen	*13*	*2*
Complications (general)		*21*
Compl dur puerperium		*2, 22*
Cord, umbilical (general)	*21*	*2, 3*
Drugs used during delivery	*5*	*21, 26, 32*
Fetal Presentation	*2*	*3, 11*
First stage	*8*	*2, 5*
Induction		*16, 34*
Medication	*8, 16, 24*	
Meconium staining	*26*	*3, 21*
Onset of labour	*26*	*2, 5*
Oxytocin	*26*	*2, 3*
Placenta (general)	*16*	*3, 52*
Resuscitation at delivery	*3, 30*	*2, 52*
Rupture of membranes	*2*	*3, 5, 13, 16, 21*
Second stage	*5, 13*	*2, 54*
Slow fetal heartbeat	*3*	
Time to discharge	*5, 13, 20, 33*	
Total duration of delivery		*2, 3, 7, 16, 24*
Type of delivery	*16, 30*	*3, 5, 7, 8, 21, 29, 32, 42, 52, 58*
Vaginal bleeding		*2, 3*

Table A3 - Factors relating to neonatal period		
Risk Factor	Study Number	
	Significant	Non-Significant
Abnormality (brain)	*2*	
Abnormality (congenital/general)	*7, 26*	*12, 29, 39*
Abnormality (liver)		*2*
Abnormality (respiratory)	*17, 29, 31, 58*	*2, 13, 21, 48, 49, 73*
Abnormal cry		*2*
Abnormal moro reflex	*3, 27, 31*	
Abnormal suck	*3*	
Apgar (1 min)	*3, 8, 29*	*2, 16, 21, 22, 52, 58*
Apgar (5 min)	*16, 69*	*2, 3, 21, 52, 58*
Appearance/ behaviour of infant	*13, 20, 31, 42*	
Bilirubin level		*3*
Blood type (infant)	*3*	*2, 52, 29, 73*
Blood type (mother)	*4, 5, 13, 26*	*7, 21, 23, 29*
Body length	*2, 8, 20, 22, 26, 30*	*3, 5, 60*
Body temperature /sweating	*3, 20, 31, 48*	*21*
Haematocritic	*2*	
Haematological problems	*27, 33*	*2*
Head circumference	*3, 8, 22, 26*	*2, 5, 23*
Hypoactivity	*26, 33*	*2, 3, 58*
Hypoglycaemia		*5*
Hypotania /floppy	*21, 26*	*2, 3*
Jaundice		*13*
Jitteriness	*3, 26*	*5*
Illness	*8, 13*	*12*
Infant feeding (problems)	*26, 27, 31, 73*	
Marked moulding of head	*3*	
Miscellaneous symptoms	*5, 27*	*21*
Neonatal cry		*2*
Neurological problem	*3, 26*	
Received antibiotics	*3*	
Received prescribed drugs	*73*	*2*
Reflexes		*3*
Respiratory distress syndrome	*3, 26, 57*	*8*
SCBU (admission to)	*5, 13, 26, 27, 44, 54, 69*	*30, 60*
Surgery (minor/ major)		*3*
Time of first breath		*2*
Vitamin K		*3*
Weight gain (infant)	*3, 27, 33*	*20*

Table A4 - Postnatal factors		
Risk Factor	Study Number	
	Significant	Non-Significant
Alcohol consumption (mother)	*8*	*29, 44, 60, 68, 73*
Alcohol consumption (partner)	*8*	*29*
Allergies (infant)		*44*
Appearance when found	*19*	
Bed contents	*49*	
Bed-type	*73*	*49, 72*
Bed-mattress filling/cover	*18, 48*	*51, 72*
Clinic visits	*5, 13, 42, 73*	
Congenital disorder of family		*3*
Depression /coping (mother)	*26*	
Dietary factors	*1*	*9*
Duvets/covers	*49*	
Exposure to fumes		*29*
Growth	*3, 7, 40, 56, 60, 68, 73*	*23*
Found with covers over the head		*48*
Heating /tog values	*29, 43, 48*	*45, 73, 49*
Housing (density)	*3, 6, 29, 54*	*2*
Housing (type)	*8, 13, 29, 48, 53*	*39, 65*
Housing (state of repair)	*13, 26*	*19, 60*
Housing (moving)	*29*	
Housing (ventilation)	*29*	*48*
Hospital admissions	*22*	*12, 39, 60*
Illegal drug use (mother)	*13, 71*	*68*
Illegal drug use (partner)		
Illness medication : Infant	*8, 13, 18, 19, 29, 42, 48*	*2, 6*
: family		
Immunisations	*25, 27, 29, 48, 73*	*21, 38, 44*
Infection	*6, 7, 27, 42, 43, 48, 73*	*2, 18, 20, 44*
Interactions (mother/baby)	*34*	
Length of last sleep	*19, 26*	
Medical history (mother)	*29, 48*	*19*
Medical history (partner)	*29*	*19*
Outside temperature		*48*
Pests		*29*
Pets		*29, 49*
Pillows	*48*	*9, 72, 73, 49*
Private Healthcare	*26*	*23*
Procedures		*2*
Roomsharing	*29, 44, 45*	
Sickness prior to death	*21, 28, 29, 42, 45, 60, 73*	*39*
Sleeping /waking problems	*20, 29*	*49*
Smoking (other)	*29, 44, 46, 47, 49, 51*	
Thymic petechiae	*26*	

Appendix III

Case Definition

All deaths occurring in the first year of life (7-364 days inclusive) that met any of the following criteria :

i) unexplained deaths (ie those meeting criteria for Sudden Infant Death Syndrome)

ii) any sudden unexpected death occurring in the course of an acute illness that was not recognised by health professionals as potentially life-threatening.

iii) any death occurring during the course of a sudden, acute illness of less than 24 hours duration in a previously healthy infant, or in an infant with a known underlying illness not directly related to the cause of death. If intensive care were instituted within the first 24 hours of such an illness, the infant was included, even if death occurred after withdrawal of intensive care more than 24 hours into the illness.

iv) deaths arising from a pre-existing condition that had not been previously recognised by health care professionals.

v) accidental and other traumatic deaths, including poisoning and deaths related to fires.

Cases were excluded where police were investigating with a view to possible criminal proceedings (against the carer) whether this occurred soon after the death or at any subsequent stage. An abbreviated enquiry was used for deaths recognised at the point of death as accidental (category V of case definition). In such deaths, questionnaire interviews were conducted but some parts of the questionnaire (e.g. those related to the infant's last sleep period) were omitted as inappropriate. Epidemiological information available from public records (sex, place and date of birth, age of parents, time and date of death, place of death, certified cause of death) was collected on all deaths.

Appendix IV

Details of prompt reporting network

In order to ensure complete and rapid ascertainment of cases all of the following sources were used in each Region:

1) General practitioners.

2) Health visitors and midwives.

3) Accident and emergency departments.

4) Ambulance and police control headquarters.

5) Local CESDI co-ordinators.

6) Hospital paediatricians and paediatric surgeons, (including those at tertiary referral centres, in different districts or different regions); hospital paediatric nurses.

7) Community paediatricians, clinical medical officers.

8) Neonatal units (N.B. in most cases deaths in neonatal units were "expected" and the confidential enquiry was thus inappropriate).

9) Coroners and coroners' officers.

10) Mortuary attendants, both hospital and civil.

11) Pathologists.

12) Hospital chaplains and community religious leaders.

13) Parent support groups, (e.g. SANDS, FSID).

The Regional and / or District Co-ordinator approached each of these groups in advance of the enquiry and explained its purpose and methods. Where appropriate, formal approaches were used, for example GPs were informed via the Local Medical Committee and the Family Health Service Authority.

A one page rapid reporting form was used to notify the case to the co-ordinating office by fax, and to provide preliminary information. Forms were widely available in clinical units to ensure complete ascertainment and documentation of cases. In addition, telephone numbers (with answer machines for out of hours) were provided for immediate reporting to the co-ordinating centres, and all involved professionals were encouraged to report all deaths for inclusion as soon as possible, even if they thought it possible that someone else may have already done so. The aim was for all notifications of deaths to be received by the SUDI offices within 24 hours of occurrence.

Appendix V

Quality control measures

(i) In-built range specifications were included for most variables on the database so that only the appropriate codes could be used for the response to each of the questions.

(ii) Guidelines were issued at the beginning of the study to each researcher within which detailed instructions were given regarding any ambiguities about the interview, questionnaire or data entry. These instructions were regularly updated.

(iii) Regular meetings were held with the researchers to discuss any queries.

(iv) Spot checks were carried out early in the study to ensure the data from the questionnaire were being entered correctly on the data base.

(v) Listings of all numerical variables entered by each researcher were printed at the end of the first year and at the end of the study and checked for missing or spurious values by at least 2 people. The listings were then sent to each researcher so that appropriate checks and corrections could be made both to the questionnaire and the listing. The corrections were then sent back to the CESDI statistician and entered onto the collective database.

(vi) All calculations made to convert dates to number of days or clothes & bedding into tog values were checked.

(vii) Social Class coding was carried out by a single person, with experience in the use of the Registrar General's classification.

(viii) Before each variable in the collective database was analysed, the responses were listed and any spurious or missing values were checked against the questionnaire.

(ix) Consistency between variables was also tested for unlikely responses, and rectified where possible. (e.g. if obstetric records listed only one pregnancy, but mother had several children).

Appendix VI

Main hypotheses to be tested

List of the 15 major areas, along with the particular variables associated within each area.

(i)	*Sleeping Position*	Prone sleeping, sleeping on side with and without arm extended, loose bedding, soft mattresses, position within the bed.
(ii)	*Thermal Environment*	Heavy wrapping, room temperature, outdoor temperature, head coverings, supplementary warming devices (eg electric blankets, hot water bottles), interactions with age or infection.
(iii)	*Smoking*	Maternal smoking during pregnancy, paternal smoking, others smoking in the household, exposure to smoky atmosphere, interaction with other markers such as socio-economic deprivation, alcohol consumption and illegal substance abuse.
(iv)	*Recent illness in the baby*	Severity of recent illness, use of healthcare resources, fevers recognised by parents.
(v)	*Bedsharing & roomsharing*	Bedsharing for part or all of the night with parents, habitual bedsharing, sleeping between parents, sharing a room but not a bed with parents, interaction with breastfeeding, illness, long-term parental smoking or recent parental alcohol consumption.
(vi)	*Dummy Use*	Apparent benefits, interactions with mode of feeding and sleeping position.
(vii)	*Breastfeeding*	Apparent benefits, interactions with maternal smoking, socio-economic status and recent illness.
(viii)	*Baby Mattress*	Risk of plastic covered mattresses, impermeable covers added by parents, interactions with prone sleeping, age of mattress and previous use.
(ix)	*Alcohol & illegal substance use*	Usual and recent parental consumption of alcohol, parental use of illegal drugs before, during and after pregnancy.
(x)	*Length of time baby was left unattended*	Infants habitually being left for long periods unattended, length of time left unattended in last 24 hours.
(xi)	*Apparent life-threatening Event (ALTE)*	Infants that have suffered a previous episode of lifelessness, apnoea, pallor or cyanosis, episodes that go unreported.
(xii)	*Maternal depression*	Depression recognised by the mother or the health professional, severe maternal depression.

(xiii)	*Previous hospital admissions or attendances*	Previous admissions to hospital, Immunisation patterns, reactions to immunisations.
(xiv)	*Previous deaths and access in emergencies*	Family history of SUDI or ALTE, support of extended family and friends, isolation in terms of lack of telephone or car.
(xv)	*Recent major life events*	Moving house recently, changes in family routine (eg holiday, long journeys, visit to friends, overnight guests etc), recent illness in the family.

Appendix VII

Details of neonatal problems

More of the index babies (23.4% vs 10.1%) were recorded as having other neonatal problems compared to the control babies (3 cases and 10 controls missing). This difference was significant (OR=2.51 [95% CI : 1.61 to 3.91]). Looking at the types of problems listed :

	SIDS	Controls
Short gestation	3	5
Jaundice	10	13
Wheezing/grunting	2	7
Cold/ hypothermia	3	4
Respiratory distress	4	5
Jittery	4	2
Heart murmur	1	5
Not feeding well	1	1
Low breast milk	2	1
Sticky eye	0	2
Narcon given	1	4
Vomiting	1	1
Asphyxia	3	1
Hip problem	0	2
Infection screen prog (SROM-NAD)	1	1
Other	9*	24**

** Transient tachypnoea, hyperbilirubin, chronic lung disease, hypoglycaemia, reluctant to straighten arm, abnormal hearing test, bilateral groin swelling, skin rash, preterm hyaline membrane disease*
*** Thrush on buttock, flat-no quick response, cephalahaematoma-facial bruising, large head, naloxone post- delivery, bruising-hypos-apnoeas-septic, umbilical stump, nasal septum, mild pyrexia, bsl at birth, gestational diabetes, right hydrocele, bloodstained stools, pyrexial swabs, low apgars due to shoulder dystoci, group b strep infection, meconium asp-pneumothorax, dilated renal pelvis, i.d.m., ingest meconium cord round x3, small swelling of right eye, hyperglycaemic, toxic erythema, low glucose.*

Congenital anomalies

Slightly more of the index infants (10.9% vs 6.6%) had congenital anomalies compared to the controls (3 cases and 10 controls missing). This difference was not significant (OR=1.73 [95% CI : 0.98 to 3.04]). The anomalies noted were as follows :

	SIDS	Control
Talipes	1	14
Abnormal digits	2	3
Birthmark	0	3
Clicky/unstable hips	2	10
Hypospadias	2	6
Spinal/sacral dimple	0	3
Cleft palate	1	1
Umbilical hernia	2	1
Skin tag/nodule on ear	0	2
Other	11*	8**

** Congenital heart, skeletal deformation, multi cystic rt kidney, Fallotsytetralogy cystic hygroma, no cartlidge in pinna, transposition of great vessels, blepharophinosis ptosis epicenthus invesus syndrome, facial palsy, 2 cord vessels only, rt duplex kidney & patent ductus*
*** Dilated kidney, tag on nipple, undescended testicles x 2, minor abnormal penis, bilateral hydrocele, micronethia, multicystic diplastic kidney.*

Appendix VIII

Quantifying illness with a retrospective scoring system

The Cambridge Babycheck is a scoring system to help parents and doctors quantify serious illness in babies upto 6 months of age. It is based on 7 symptoms and 12 signs, each of which receives a score if they are evident, the higher the score the more ill the baby.

Question	Score	
Have these symptoms been present in the last 24 hours?		
1) Has the baby vomited at least half the feed after each of the last 3 feeds?	*4*	
2) Has the baby had any bile-stained (green) vomiting?	*13*	
3) Has the baby taken less fluids than usual in the last 24hrs?		
If so score for the total amount of fluids taken as follows :		
Taken slightly less than usual (more than 2/3 normal)	*3*	
Taken about half usual amount (1/3-2/3 normal)	*4*	
Taken very little (less than 1/3 normal)	*9*	
4) Has the baby passed less urine than usual?	*3*	
5) Has there been any frank blood (not streaks) mixed with the baby's stools?	*11*	
6) Has the baby been drowsy (less alert than usual) when awake?		
If so, score as follows:		
Occasionally drowsy (but usually alert)	*3*	
Drowsy most of the time (occasionally alert)	*5*	
7) Has the baby had an unusual cry (sounds unusual to mother)?	*2*	
Now examine the baby awake		
8) Is the baby more floppy than you would expect?	*4*	
9) Talk to the baby. Is the baby watching you less than you expect?	*4*	(Not asked)
10) Is the baby wheezing (not snuffles or upper respiratory noises) on expiration?	*3*	
11) Is the baby responding less than you would expect to what is going on around?	*5*	(Not asked)
Now examine the baby naked for the following checks		
12) Is there any indrawing (recession) of the lower ribs, sternum or upper abdomen? If so, score as follows:		
Just visible with each breath?	*4*	
Obvious and deep indrawing with each breath?	*15*	
13) Is the baby abnormally pale or has the baby looked very pale in the last 24 hours?	*3*	
14) Does the baby have blue fingernails or toenails?	*3*	
15) Squeeze the big toe to make it white. Release and observe colour for 3 seconds. Score if the toe is not pink within 3 seconds, or if it was completely white to start with?	*3*	(Not asked)
16) Has the baby got an inguinal hernia?	*13*	*
17) Has the baby an obvious generalised trunkal rash or a sore and weeping rash covering an area greater than 5x5cm?	*4*	
18) Is the baby's rectal temperature 38.3°C or more?	*4*	**
19) Has the baby cried (more than just a grizzle) during this assessment?	*3*	(Not asked)

* The questionnaire did not specifically ask if the baby had an inguinal hernia but did ask if the baby had any illness in the last week and also any hospital admissions.

** Not being able to get the index baby's rectal temperature both index and control mothers were asked whether the baby had a fever in the last week.

All but 4 of the questions were asked retrospectively in the questionnaire in the same format as detailed in the Cambridge babycheck.

The scores are grouped and action is linked to each group :

Score 0 to 7	Baby is generally well.
Score 8 to 12	Baby is unwell but not seriously ill, get health advice and observe baby
Score 13 to 19	Baby is ill and needs a doctor
Score 20+	Baby is seriously ill and needs a doctor straight away

The maximum score possible using the Babycheck is 111, the maximum possible score using the revised Babycheck of the questionnaire is 96. Care must therefore be taken when interpreting the revised babycheck results as these will be an underestimate of the baby's health.

Analysis of the Individual Questions

1) Has the baby vomited at least half the feed after each of the last 3 feeds?

Table A8.1 shows that twice as many index babies vomited in the last 24 hours compared to the controls and that this difference was significant.

Table A8.1 - Vomiting in the last 24 hours					
	SIDS		Controls		OR [95% CI]
Vomiting in last 24hrs	N=192	%	N-777	%	
No	151	78.6	700	90.1	1.00 [Ref Group]
Yes	41	21.4	77	9.9	2.47 [1.58 to 3.81
Number of times	N=190	%	N=776	%	
None	151	79.6	700	90.4	1.00 [Ref Group]
1 or 2 times	25	13.6	50	6.4	2.72 [1.36 to 5.26]
3 or more	13	6.8	25	3.2	2.41 [1.10 to 5.02]
At least half of feed	N=190	%	N=776	%	
None	171	90.0	739	95.4	1.00 [Ref Group]
1	10	5.3	14	1.8	3.09 [1.20 to 7.61]
2 or more	9	4.7	22	2.8	1.77 [0.7 to 4.08]

The mothers were also asked how many times the babies vomited in the last 24 hours. The number ranged from none to 12. Looking at babies that only vomited once or twice and those that vomited 3 times or more, vomiting was more frequent in the index group. The mothers were also asked how many of these vomits were at least half a feed. The number ranged from none to eight. Significantly more of the index infants had one or more such episodes (OR=2.28 [95% CI : 1.20 to 4.20]). The risk associated with these episodes did not increase with the number of episodes. In terms of the revised Babycheck, only 4 cases and 4 controls vomited half feeds or more in the last 3 feeds.

2) Has the baby had any bile-stained (green) vomiting?

Only 4 index infants and 2 control infants had bile-stained vomit. This difference was significant (p=0.017).

3) Has the baby taken less fluids than usual in the last 24hrs?

Three times as many index babies took less fluids in the last 24 hours compared to the controls, this difference was significant (OR=3.50 [95% CI : 2.21 to 5.49]).

Table A8.2 - Less fluids in the last 24 hours					
	SIDS		Controls		OR [95% CI]
Less fluids	N	%	N	%	
No	149	77.6	716	92.4	1.00 [Ref Group]
Yes but > 2/3rds	23	12.0	41	5.3	2.70 [1.49 to 4.75]
Yes about 1/2	13	6.8	11	1.4	p=0.00006*
Yes < 1/2	7	3.6	7	0.9	p=0.006*
* Fisher's exact test As a single paramater on 3 degrees of freedom p<0.001 N−192 SIDS & 775 Controls					

Although the numbers were small, if we look at the decreasing quantity taken in each group compared to the reference group, the difference was significant for each group.

4) Has the baby passed less urine than usual?

Although the numbers were small, significantly more of the index babies (7.5% vs 3.5%) passed less urine compared to the controls (OR−2.26 [95% CI : 1.07 to 4.57]).

5) Has there been any frank blood (not streaks) mixed with the baby's stools?

Only 1 baby had blood in their stools, and this was a control infant.

6) Has the baby been drowsy (less alert than usual) when awake?

Three times as many index mothers (11.3%) noticed that their baby had been less alert than usual compared to the control mothers (3.7%). This difference was significant (OR=3.31 [95% CI : 1.76 to 6.12]).

7) Has the baby had an unusual cry (sounds unusual to mother)?

More of the index mothers noticed an unusual cry from the baby in the last 24 hours (13.5% vs 5.4%) compared to the control mothers. This difference was significant (OR=2.73 [95% CI : 1.56 to 4.70]).

8) Is the baby more floppy than you would expect?

A small number of index mothers noticed that their child was floppy (4.2% vs 1.4%), significantly more than the controls (p=0.04).

10) Is the baby wheezing (not snuffles or upper respiratory noises) on expiration?

Significantly more of the index babies (17.0% vs 8.6%) wheezed on expiration compared to the controls (OR 2.18 [95% CI : 1.34 to 3.48]).

12) Is there any indrawing (recession) of the lower ribs, sternum or upper abdomen?

A similar proportion of index cases (16.0%) appear to have had an indrawing of the lower ribs compared to the control babies (14.3%). There was no significant difference (OR=1.35 [95% CI : 0.84 to 2.11]). Neither was there any difference when these signs were broken down into just visible signs (p=0.49) or obvious signs (p=0.61).

13) Is the baby abnormally pale or has the baby looked very pale in the last 24 hours?

Three times as many index mothers thought their baby looked abnormally pale in the last 24 hours (10.5% vs 3.5%) compared to the control mothers. This difference was significant (OR = 3.24 [95% CI : 1.68 to 6.15]).

14) Does the baby have blue fingernails or toenails?

Very few babies had abnormally blue fingernails or toenails, this was observed in a small but significant proportion of the index cases (2.6% vs 0.8%) compared to control infants (p=0.047).

16) Has the baby got an inguinal hernia?

The mother was asked whether the baby had any illness in the last week before death. The main illnesses described included crying, not settling, teething, coughing, colds, chest infection, sticky eyes, conjunctivitis, ear infections, diarrhoea, vomiting, eczema and skin rash. There was no difference between the two groups, inguinal hernia was not mentioned. The mother was also asked about previous hospital admissions. One index mother and 3 control mothers mentioned treatment for an inguinal hernia, only one said that the baby was still waiting for this operation. This was a control baby.

17) Has the baby an obvious generalised trunkal rash or a sore and weeping rash covering an area greater than 5x5cm?

Slightly more of the index babies (9.8°o vs 6.3%) had a rash compared to the control infants, but this difference was not significant (OR=1.63 [95% CI : 0.88 to 2.90]). The great majority of the rashes were described as nappy rashes.

18) Is the baby's rectal temperature 38.°C or more?

The parents were asked whether the baby had a fever in the last week. If so, was the baby's temperature measured, what with, how and what was the temperature. More of the index babies had a fever in the last week (14.7% vs 10.3%), but the difference was not significant (OR=1.49 [95% CI : 0.90 to 2.41]). Unfortunately, the temperature was measured in less than a third of both cases and controls, and of those that gave readings only 2 cases and 4 controls had temperatures of over 38.3°C. The Babycheck takes the rectal temperature of the baby during assessment. As the temperature for two thirds of the babies was not known and both the accuracy and the period in which temperatures were taken cannot be clarified, the temperature data was unreliable. However the questionnaire did ask if the infant had a fever in the last week. This could be used as a rather crude proxy measure, analysing the revised Babycheck score both with and without this variable.